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DISEASES of CHILDREN

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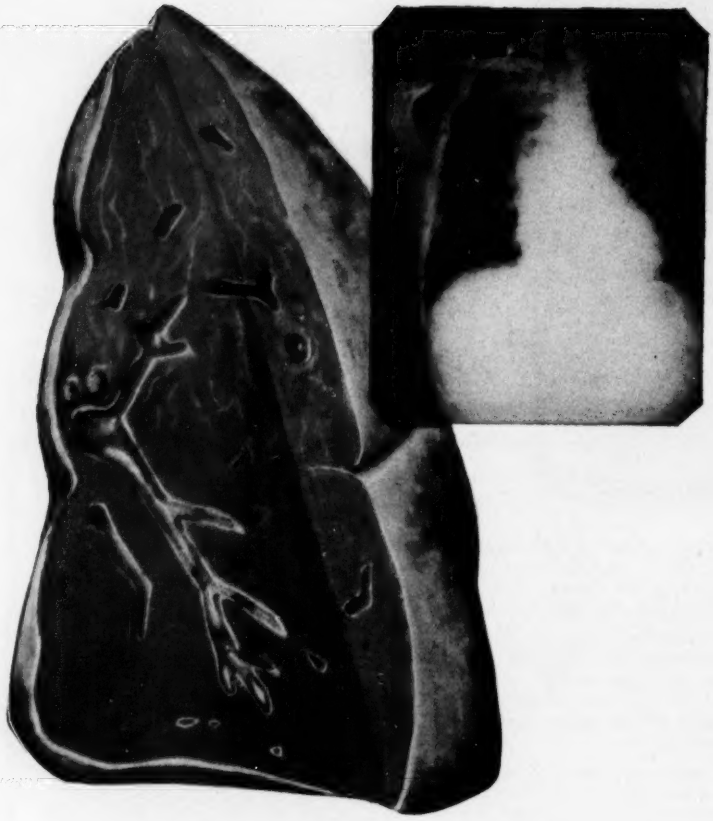

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1. Graves, F. B., and Ball, W. O.: J. Pediat. 39:155 (Aug.) 1951.

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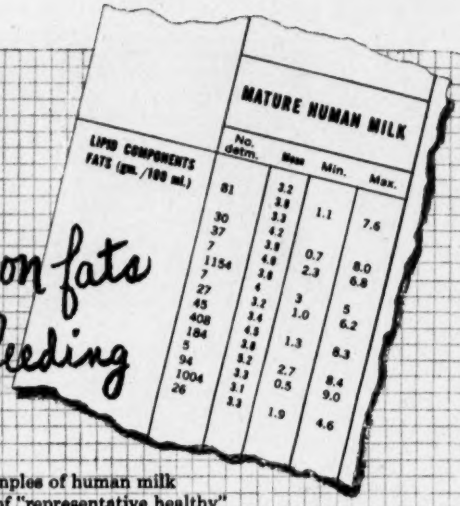

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	81	3.2		
		3.8		
	30	3.5	1.1	7.6
	37	4.2		
	7	3.8		
	1154	4.0	0.7	
	7	3.6	2.3	8.0
	27	4		6.8
	45	3.2	3	
	408	3.4	1.0	5
	184	4.3		6.2
	5	3.8	1.3	
	94	3.2		8.3
	1004	3.3	2.7	
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1. Muller-Stephann, H.: Ztschr. Kinderheilk. 67:495, 1950.
2. Salmi, T.: Acta Paediatrica 32:7, 1944.

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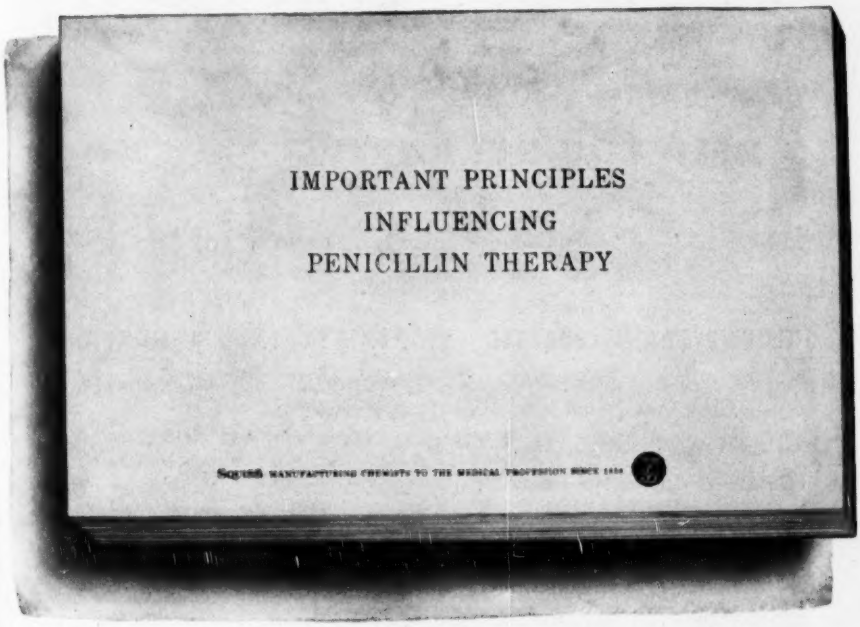

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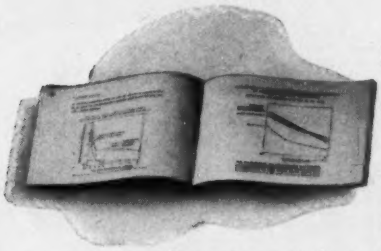

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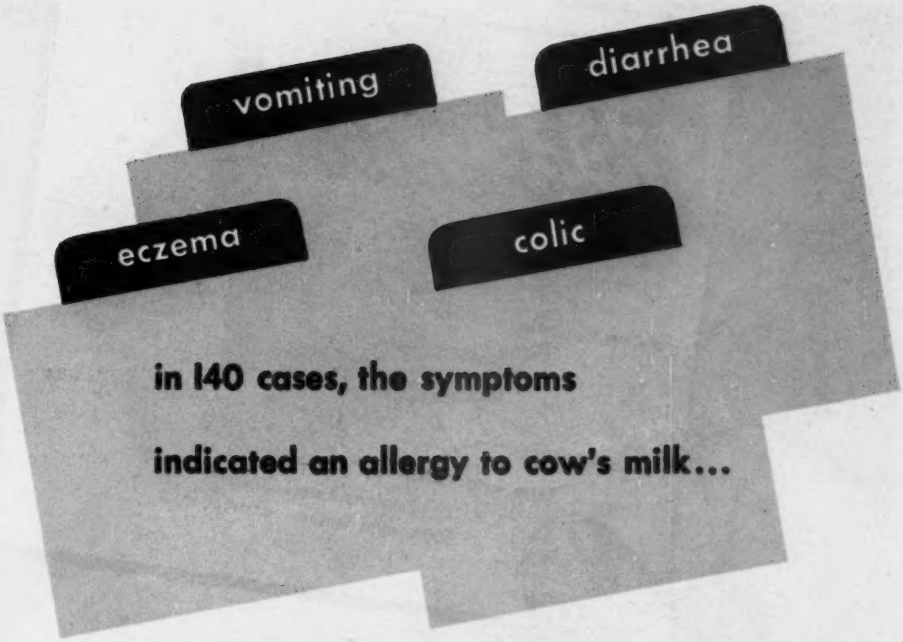

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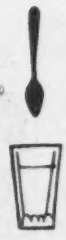

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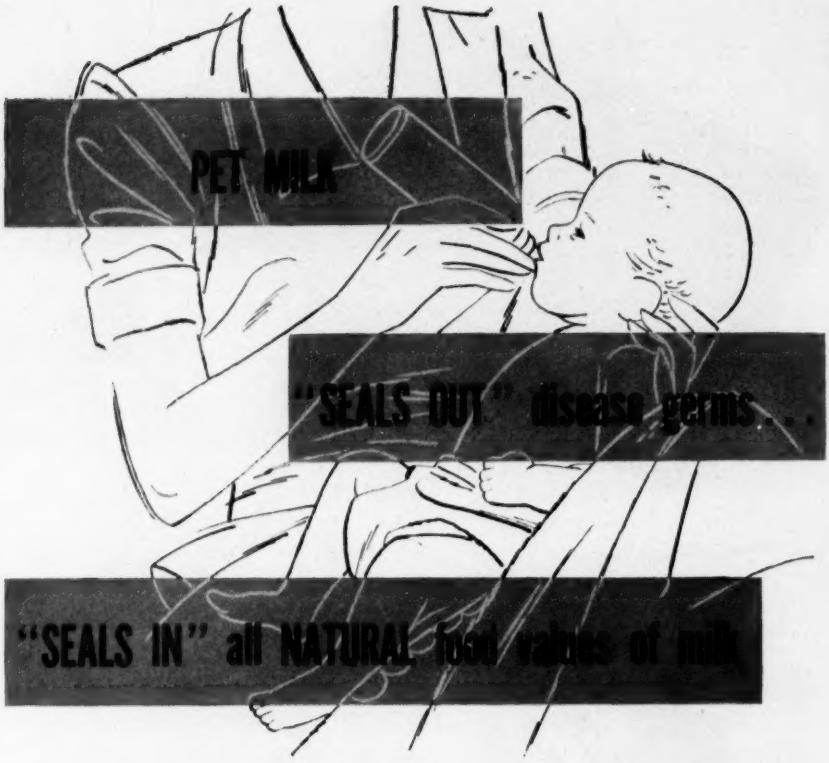

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VOLUME 83 MARCH 1952 NUMBER 3

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CAUSE AND SEQUELAE OF INTRAPULMONARY SHADOWS IN PRIMARY TUBERCULOSIS

G. M. H. VEENEKLAAS, M.D.
UTRECHT, NETHERLANDS

I. Cause of Intrapulmonary Shadows in Primary Tuberculosis

PRIMARY type pulmonary tuberculosis is considered to be principally a disease of the lungs. The great importance of the bronchi has received little attention. Their role is probably most clearly demonstrated by cases in which lobar or segmental shadows are presented. A review of present knowledge concerning these shadows follows.

In 1920 Eliasberg and Neuland [1] described a large shadow in the lungs of a few children who were not very ill and had positive tuberculin reactions. This shadow was of an even density, wedge-shaped, with its apex toward the hilus, and covered the area of an entire lobe.

Starting from the periphery, the process of clearing-up may take from a few months to more than a year. These shadows were most frequently found in the middle or upper lobes. A similar shadow may also be caused by caseous pneumonia. Which of these two diseases actually existed became evident by the clinical course; a sharp distinction was always made between the two forms by it. Later it was found that these shadows may cover a pulmonary segment only.

Among the relatively scarce autopsy findings, two lesions were found as a cause for these shadows. There was either a proliferative epithelioid cellular pneumonia with little caseation and softening [2] or unspecific inflammation with specific foci, combined with atelectasis.[3]

Pathological, bronchographic, and bronchoscopic investigations in recent years have revealed that the shadows are caused by bronchial obstruction, either because a tuberculous lymph node [4] involves the bronchial wall in the disease process or because it perforates into the bronchial lumen.[4] Tuberculosis of the bronchial wall causes edema; hyperemia; submucous tuberculomas; ulceration; perforation, resulting in small fistulas (one or more) or in a large opening; and after perforation, formation of granulation tissue. With sufficient narrowing of the bronchus, natural

From the University Pediatric Department (Head, Prof. Dr. A ten Bokkel Huinink), Wilhelmina Children's Hospital.

1. Eliasberg, H., and Neuland, W.: Jahrb. Kinderh. **93**:88, 1920.

2. MacGregor, A. R., and Alexander, W. A.: Edinburgh M. J. **44**:561, 1937. Schwartz, P.: Empfindlichkeit und Schwindsucht, Leipzig, Johann Ambrosius Barth, 1935.

3. Rössle, R.: Virchows Arch. path. Anat. **296**:1, 1935. de Bruin, M.: Arch. Dis. Childhood **11**:65, 1936.

4. (*a*) Jones, E. M.; Rafferty, T. N., and Willis, H. S.: Am. Rev. Tuberc. **46**:392, 1942. (*b*) Kent, E. M.: ibid. **46**:524, 1942. (*c*) Göttche, O. G., and Kassay, D.: Ann. pædiat. **168**:245; 311, 1947. (*d*) Hutchison, J. H.: Quart. J. Med. **18**:21, 1949.

drainage becomes impaired. Secondary inflammation will easily arise behind the obstruction (obstructive pneumonitis, obstructive pneumonia). The perforated lymph node may contain tubercle bacilli. When these are aspirated, they may cause tuberculous foci in the area beyond the obstruction. Moreover, the primary focus is often situated in the shadowed area.

With a certain degree of obstruction, air may be sucked in at inspiration but not be blown out at expiration, and thereby emphysema is caused.[5]

Tubercle bacilli are found remarkably seldom in the contents of a tuberculous lymph node.[6] It is also noteworthy that perforated caseous material teeming with tubercle bacilli need cause no demonstrable dissemination.[4d]

Bronchiectases have been described as the residue of these shadows.[7] These were mostly situated in the upper lobes and caused no symptoms, probably because of natural drainage. In a few instances stenosis was observed as a remnant of a lobar shadow.[8] Lately bronchoscopic removal of obstructive granulation tissue and caseous masses has been recommended, with aspiration of the retained mucopus.[9] After this procedure, the shadow is sometimes seen to diminish considerably or to disappear entirely in a few days to a few weeks.

RESULTS OF PERSONAL OBSERVATIONS

Personal observations[10] confirm to a large extent the above description but differ in certain respects. According to observations that I have made, lobar and segmental shadows are frequent lesions in children. They were found to exist in 35 of 102 patients with primary type pulmonary tuberculosis who entered the pediatric department of the Utrecht University Hospital. Their ages varied from 6 months to 12 years. They were not specially selected, but it should be borne in mind that patients admitted to a university hospital are likely to be selected to a certain extent.

One-third of the patients were severely ill, with high fever which often persisted for weeks or months.

Clearing of the shadow sometimes started in a few months, sometimes after several years, but nearly always took over a year to become complete. These findings are in some contradiction to data from the literature.

Lobar shadows were sometimes attended by multiple cavities within these shadows. In such cases the children were severely ill, and the disease ran such a protracted course that in earlier years it would with certainty have been diagnosed

5. Eliasberg, H.: Jahrb. Kinderh. **139**:12, 1933. Priesel, R.: Fremdkörper im Luftwege bei Kindern, Ferdinand Enke, Stuttgart, 1935. Spivek, M. L.: Obstructive Pulmonary Emphysema Due to Partial Obstruction of Bronchi by Tuberculous Lesions, Am. J. Dis. Child. **51**:69 (Jan.) 1936. Faust, O. A.: Primary Tuberculosis, Obstructive Pulmonary Emphysema and Asthma with Recovery, ibid. **51**:118 (Jan.) 1936. von Sydow, G.: Acta pædiat. **26**:465, 1939. Barsby, B.: Lancet **1**:627, 1941. Meneghello, J., and Smith, C. A.: J. Pediat. **22**:265, 1943.

6. Kraan, J. K., and Muller, S.: Acta tuberc. scandinav. **24**:88, 1950.

7. Jones, E. M.; Peck, W. M., and Willis, H. S.: Bronchiectasis Following Primary Tuberculosis, Am. J. Dis. Child. **72**:296 (Sept.) 1946.

8. Lightwood, R., and Wilson, R.: Arch. Dis. Childhood **11**:321, 1936. Graham, S., and Hutchison, J. H.: ibid. **22**:162, 1947.

9. Roberts, J. C., and Blair, L. G.: Lancet **1**:386, 1950.

10. Veeneklaas, G. M. H.: Geneesk. bl. klin. en lab. prakt., pp. 1-191, 1950.

as caseous pneumonia. This certainty is now lacking because with streptomycin and paraaminosalicylic acid treatment, these patients are cured and their cavities disappear in a few months. Here, also, the cause appeared to be an obstructing process in the bronchus, while the remaining lesions did not differ from those found after lobar shadows without cavitation. Whether these were tuberculous or nonspecific cavities is a hard question to answer. The result of the examination of the fasting-stomach washings is variable, being sometimes constantly negative and at other times constantly positive, but this result is also influenced by the bronchial lesion. The extremely grave condition of the children, which closely resembles phthisis, inclines the observer to assume that tuberculous cavities exist. The question arises, however, of whether it is possible for cavities of a tuberculous nature to disappear in a few months under the influence of treatment.

Removal of the obstruction and aspiration are indicated as logical. However, immediate results are in most cases still questionable, and ultimate results are not yet known.

Patients are often confined to their beds until their shadows have nearly or entirely disappeared. We found that these patients can be gradually but completely mobilized, regardless of the continued existence of shadows, once their temperature and sedimentation rate remain at values below 37.1 C. (98.8 F.) and 10 mm., respectively, for a period of three months.

From the above discussion it is evident that perforation of a lymph node into a bronchus is often the underlying lesion in lobar and segmental shadows. Like Dufourt and Mounier-Kuhn,[11] we have observed small fistulating perforations in the bronchi, unaccompanied with such intrapulmonary shadows. Perforation of tuberculous lymph nodes apparently occurs more frequently than clinical observation leads one to suspect. Autopsy findings have given similar indications. On the basis of these observations, the following hypothesis is advanced. With increasing firmness of the contents of the lymph node and increasing narrowness of the bronchi, obstruction will occur more and more easily after rupture. However, the contents of the tuberculous nodes are often liquid, and the bronchi widen with advancing age. The frequency of primary tuberculosis also increases with age; therefore, it may evidently be assumed that many of these perforations occur unnoticed and that only the minority of these cause lobar or segmental shadows. Considering the frequency of such shadows,[10] in connection with the above-mentioned facts, it may be concluded that rupture of lymph nodes into the bronchi is a frequently occurring process. This line of thought may lead to still other conclusions. The shadows described are the result of lymph node rupture only under certain conditions. But this same rupture will be the result of tuberculosis of a lymph node also only under certain conditions. In a large number of cases the bronchial wall may be involved in some way in the tuberculous process without its leading to a perforation of the tuberculous node into the bronchus. This becomes even clearer in considering the fact that tuberculosis generally extends via the primary focus in the periphery of the lung along the peribronchial lymph vessels toward the lymph nodes along the bronchi. This will cause clinical signs in the minority of cases. To put it differently, it is probable that primary tuberculosis of the lung is accompanied with some form of tuberculosis of the bronchus.

11. Dufourt, A., and Mounier-Kuhn, P.: Rev. tuberc. **11**:155, 1947.

The lobar and segmental shadows under discussion were found to be the result of a tuberculous lesion of the bronchus with a component of secondary inflammation. I found that many shadows resemble the lobar and segmental shadows in cause

Fig. 1 (girl 2 years).—Left, a wedge-shaped homogeneous shadow is seen in the right upper lobe. Right, the cause of the shadow is a block in the right upper lobe bronchus.

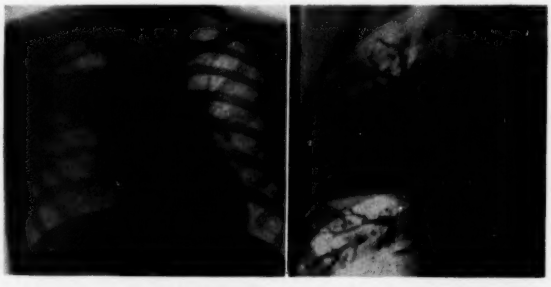

Fig. 2 (girl 9 years).—Left, shadows are seen in the pectoral and paravertebral segments of the right upper lobe. Right, no iodized oil enters the bronchi of the shadowed segments.

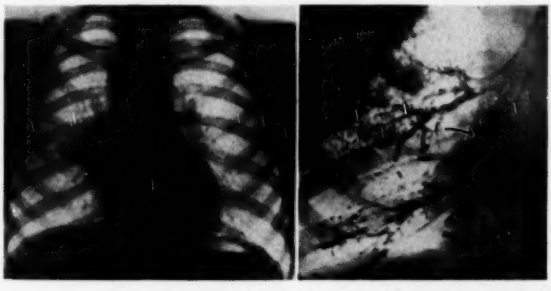

Fig. 3 (girl 10 years).—Left, at the right a perihilar shadow not typical for the size of a lobe or segment is seen. Right, the shadow is nevertheless caused by granulomatous tissue (arrow).

and behavior but not in shape. The question then arises if not most or all of the intrapulmonary shadows in primary tuberculosis develop as the result of a tuberculous bronchial lesion. Of course, not included are the primary focus developing aerogenously, hematogenous spreads, and some perihilar shadows developing as

the direct result of a diseased lymph node acting on the lung tissue. Confirmatory evidence is available in support of the hypothesis that all other shadows in primary type tuberculosis are bronchogenic.

The following examples are given:

1. A wedge-shaped homogeneous shadow, the size of a lobe, is accompanied with obstruction of the bronchus aerating this area (Fig. 1).

2. Segmental shadows in a lobe are accompanied with serious lesions of the relevant bronchi. Iodized oil did not enter these bronchi (Fig. 2).

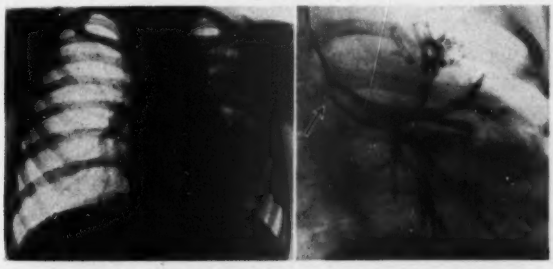

Fig. 4 (girl 6 years).—Left, unilateral, varying shadows are found in the left lung; bronchogenic spread was caused by perforation in the left stem bronchus. Right, stenosis of the left stem bronchus occurred as a sequel of the perforation at this point (arrow).

Fig. 5 (boy 2 years).—Left, a tomogram reveals multiple cavities in the shadowed left upper lobe. Right, the cause of the shadow is a block in the left upper lobe bronchus; just above the block a perforation hole of a lymph node in the left stem bronchus (arrow) is seen.

3. An atypical shadow is associated with serious lesions of a relevant bronchus. The filling defects in the iodized oil shadow were caused by tuberculous granuloma in the right primary bronchus at the point where the middle lobe bronchus branches off (Fig. 3). After removal of this, the opacity became smaller within a few weeks.

4. Dissemination exclusively in the left lung was caused by perforation of a lymph node in the left primary bronchus. At the site of this perforation a stenosis developed (Fig. 4).

5. A lobar shadow existing in a gravely ill patient, with cavities in the shadow and persistently positive sputum, was accompanied with plugging of the left upper lobe bronchus, as proved by bronchography (Fig. 5).

On the basis of these theoretical considerations and personal observations, illustrated by examples, it would seem to be probable that (1) primary type pulmonary tuberculosis is generally tuberculosis of the bronchial wall; (2) the origin of intrapulmonary shadows in primary type pulmonary tuberculosis, with the exception of the primary focus, hematogenous disseminations, and certain perihilar shadows, is to be found in tuberculosis of the bronchial wall.

SUMMARY

Greater significance should be assigned to the bronchi in the development of primary type pulmonary tuberculosis.

Data from the literature, theoretical considerations, and personal observations have led to the conclusion that the bronchi are probably involved in the majority of cases of primary type pulmonary tuberculosis, and that pulmonary shadows are generally the result of bronchial lesions. Rupture of lymph nodes into the bronchi is more frequent than is clinically apparent.

II. Sequelae of Intrapulmonary Shadows in Primary Tuberculosis

Only a few of the patients with lobar or segmental shadows in the lung during a primary tuberculous infection have been subjected to a follow-up examination. Jones [7] examined 32 children four years after the shadow had first been discovered, and in 24 of them bronchiectases were found, generally in the upper lobes and causing no symptoms.

Of a total of 101 patients presenting such shadows, I could subject 51 to a follow-up examination, 26 from 1 to 5 years, 25 from 5 to 16 years after the discovery of the shadow. No significant differences appeared to exist between the two groups. A roentgenogram of the thorax was made and bronchography was done in these 51 cases. In 21 of the patients nothing abnormal was found. In the other 30 the following changes were observed: 12 had stenosis of primary, lobar, or segmental bronchus; 15 had rigidity or ectasia of the bronchi of a lobe or a segment; 5 had deformation of bronchi; 5 had marked shrinking of a lobe; 5 had marked hypertrophy of bronchi of other lobes, and 7 had thickening of the pleura (interlobar).

These lesions were found 10 times in the right upper lobe, 7 times in the left upper lobe, 8 times in the middle lobe, 4 times in the lingula, and once in the left lower lobe, corresponding with the original localization of the shadow.

The incidence distribution is determined by the site of the primary complex and the localization of the bronchial lymph nodes.

The lesions described, except the last one, were found either with or without a roentgenological shadow. It is of great practical significance that large lesions of the bronchi may exist and still give a normal or almost normal roentgenogram.

Apparently, lobar and segmental shadows in primary pulmonary tuberculosis may cause a variety of lasting changes. But these changes often remain symptomless.

Fifty of the 51 patients had remained without symptoms since their discharge from hospital or sanatorium. Only one of them, with bronchiectasis of the left lower lobe, had low-grade fever and rales.

The question of whether the resulting lesions will remain symptomless throughout life has been presented by myself elsewhere.[10] Considering a recent publication by Brock,[12] they may indeed be the cause of severe symptoms (such as hemoptysis and recurrent pneumonia) in adult life and even at an advanced age.

To the treatment of these lesions, which used to consist in bed rest and adequate nutrition, bronchoscopic removal of the tuberculous tissue which narrows the bronchus is now added. However, insufficiently accurate knowledge concerning the frequency of residual lesions in the bronchi under the old method of treatment may possibly be an obstacle in the proper evaluation of the results of the new one.

LESIONS FOUND

A few remarks on some of the lesions may be added.

Stenosis.—Stenosis appeared to be hardly less frequent than bronchiectasis, which fact is not recorded in the literature. Bronchiectasis is frequently described, stenosis rarely; unless stenosis is of a certain degree or causes symptoms, it may

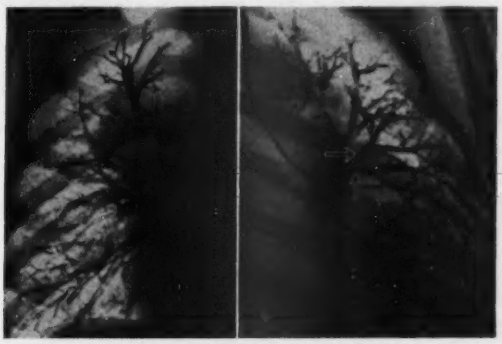

Fig. 6.—Left (boy 8 years), various stenoses appear in the right upper lobe bronchus and branches; three years previously a shadow of the entire right upper lobe had been detected. Right (boy 13 years), a few small ectatic areas of the pectoral bronchus (horizontal arrow) and slight stenosis of the lingular bronchus are shown; four years previously a shadow of the left middle region and a block of the lingular bronchus had been found.

escape notice more easily than bronchiectasis. We have never observed any symptoms. Bronchoscopic inspection may reveal considerable stenosis, accompanied with no retention beyond the site. Stenoses may be seen in bronchi of the fourth and fifth order.

We have not yet been able to study the course of an individual stenosis over a number of years. It seems likely that stenosis, rather than ectasia, will give rise to symptoms in the long run.

At the left of Figure 6 is shown stenosis of the bronchus of the right upper lobe and of the pectoral segment and ramifications of it. These were the findings in an 8-year-old boy who had presented a shadow in the right upper lobe three years previously. He had no symptoms, and the epithelium of the right upper lobe bronchus, also visible beyond the stenosis, appeared entirely normal bronchoscopically.

12. Brock, R. C.: Thorax **5**:5, 1950.

Rigid Bronchi and Bronchiectases.—Between these two there is only a gradual difference. They are frequent residual lesions and are often found beyond the stenoses.

They may occur in bronchi of any caliber. In my cases they were clinically without symptoms, not only when localized in the upper lobe, but also when situated in the middle lobe or the lingula. In the one patient with lower lobe localization they were accompanied with the well-known signs. Drainage of the upper lobes is continuous, of the lingula and the middle lobe only nocturnal, but it never occurs in the lower lobe. Symptoms may be expected to decrease in inverse order.

Symptoms of post-tuberculous bronchiectasis of the lower lobe have indeed been observed before and also in children. Brock [12] drew attention to post-tuberculous bronchostenosis and bronchiectasis of the middle lobe. His material is confined to adults. Symptoms following middle lobe lesions seem to be considerably more frequent than those following involvement of the upper lobes.

Fig. 7.—Left (boy 12 years), shrinking of the right upper lobe and bronchi is shown; there is considerable growth of the right middle lobe bronchi upward; thus, a part of the upper lobe is replaced; a shadow of the right upper lobe was present 11 years previously. Right (youth 19 years), the middle lobe is shrunken to a small bronchiectatic pouch; the bronchi of the upper lobe have grown downward, thus replacing the middle lobe; a shadow of the right middle lobe was seen 13 years previously.

We definitely gained the impressions that ectatic bronchi may recover a normal lumen and that wide ectatic bronchi, especially those in young persons, may decrease in diameter.

Bronchiectases in the pectoral, i. e., the lowest segment of the upper lobe, are a very frequent residual condition following a consolidation of the entire right upper lobe.

Irregular Mutilation.—The lesions here involved are a combination of discrete stenosis and ectasia, easily escaping detection, but not very rare. They may be associated with frank stenosis or ectasia, but may also occur singly. At the right of Figure 6 an example of this in a boy aged 13 years is shown. Four years previously there was a shadow in the left middle area, and the bronchogram revealed a block in the lingula-bronchus.

Now there are stenoses in the lingula-bronchus and in one of its ramifications, while in the bronchus of the pectoral segment there are a few small ectatic areas.

Shrinking and Growth.—These processes occurred repeatedly in an area of bronchial lesions if sufficient fibrosis had set in.

If a large area is involved, for instance a whole lobe, the loss of volume may be considerable, only a small part of the lobe remaining. Emphysema might be expected in the other lobes, but I was never able to diagnose it in my patients. As there was also no reduction in the size of the involved half of the thorax, in any phase of respiration, growth of the unaffected part of the lung could be assumed. In accordance with this, the bronchi change their course and become longer. Only pronounced cases, which are illustrated in Figure 7, have been chosen for comment. The bronchogram at the left of Figure 7 is that of a 12-year-old boy who had a shadow in the right upper lobe 11 years previously. The upper lobe bronchus and the ramifications have become a narrow bundle, parallel with the trachea. The upper lobe must have become very small, its original area being largely taken up by the middle lobe, of which the bronchi have become much longer and curved upward.

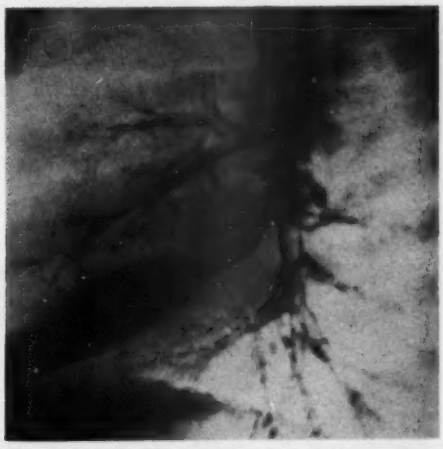

Fig. 8 (boy 6 years).—Rigid and slightly ectatic bronchi are seen in the shadowed and diminished middle lobe; a shadow of the right middle lobe had been encountered five years previously.

At the right of Figure 7 is a bronchogram for a youth of 19 years in whom a density of the right middle lobe was found 13 years ago. This middle lobe has now shrunken to a small, slightly bronchiectatic pouch, while the bronchi of the upper lobe incline toward the area of the middle lobe.

SIGNIFICANCE OF SOME OF THE SHADOWS

Shadows with the same localization will clear up in an identical way. This is especially true for shadows of the right middle and left upper lobes. For both a certain residue of the shadows often persists for many years. Sometimes the bronchi are situated in this remainder, more frequently outside of it. In the first case described there is without doubt an intrapulmonary fibrosis. In the second the remaining shadow appears as a pleural thickening when the middle lobe is involved.

This is more difficult to say with certainty for the remaining shadow of the left upper lobe, because a different position of the pleura excludes the possibility of an

identical roentgenological appearance. By analogy with a similarly remaining shadow of the middle lobe, it may be assumed that in a case of persisting shadow of the left upper lobe, thickening of the pleura is also of great importance. It will not always be possible to differentiate very sharply between fibrosis of the pleura and that of the lung, and fibrosis of the two will often occur together.

Figure 8 shows rigid and slightly ectatic bronchi in a shadowed and diminished middle lobe. This condition was encountered in a boy of 6 years in whom five

Fig. 9 (boy 6 years).—Left, a small remnant of the shadow of the right middle lobe presented five years previously is seen. Right, rigid bronchi lie outside the shadowed area. Probably the shadow was caused by pleural thickening.

Fig. 10.—The paravertebral shadow on the left was frequently found as a remnant of a shadow of the left upper lobe and is probably caused by pleural thickening.

years previously a shadow of the middle lobe had been discovered. Figure 9 concerns a child of 6 years who also had presented a shadow of the right middle lobe five years previously. There is still a narrow shadow to be seen in this area (left), but the rigid, slightly ectatic bronchi are found clearly to lie outside this area (right). Figure 10 shows a striped shadow to the left of the spine. We have often noticed that the shadow which once entirely covered the left upper lobe has retracted to this size in the course of a few months. The bronchi, either mutilated or normal, were with one exception always lying outside this shadow, which could

be described as characteristic. On the basis of this observation and by analogy with the findings for the middle lobe, I am inclined to regard this shadow as a pleural thickening.

SUMMARY

Marked residual lesions of the bronchi are found after primary pulmonary tuberculosis. They are usually symptomless and occur without or with only slight changes in the chest roentgenogram. In 30 of 51 patients with lobar or segmental shadows these were found 1 to 16 years after the discovery of the original shadow. The principal findings were stenoses, ectasia, severe shrinking, and marked growth.

With one exception these lesions were found in the upper lobes, the middle lobe, and the lingula. They did not give rise to any symptoms. The one exception, the patient with stenosis and ectasia of the lower lobe, had symptoms. The lesions are described in detail.

The residual shadows in the right middle lobe and the left upper lobe are probably often to a large extent due to pleural thickening.

ELECTROCARDIOGRAPHIC FINDINGS IN MEASLES

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NEW YORK

EVIDENCE that myocarditis can occur in several diseases of viral etiology has been accumulating and has been summarized by Lyon [1] and by Saphir.[2] There have been a few reports indicating that measles is one of the virus diseases which occasionally may be associated with cardiac disturbance.

It is questionable whether anatomical changes in the heart occur during measles. In 1937 Degen [3] described the findings in 100 autopsies of patients who died while ill with measles. There were four instances of pericarditis, and four of the 91 hearts examined microscopically demonstrated "more than the usual toxic changes." Since many of the patients also had secondary bacterial infections, it is difficult to tell whether any of the cardiac pathologic changes were attributable to the measles virus.

Clinical and/or electrocardiographic findings suggestive of cardiac disturbance in measles have been observed in a few instances. Hecht [4] described the case of a 3-year-old girl who showed conduction disturbances (2:1 heart block, Wenckebach's phenomenon, and first-degree heart block) on electrocardiograms taken during the third week after she had had measles probably complicated by influenza. Neubauer [5] noted the presence of myocarditis, during the febrile stage, in four patients who had measles and bronchopneumonia. A patient reported by Lyon [6] first sensed arrhythmical beating of his heart when he had measles at the age of 39; he had paroxysmal bouts of tachycardia during the following two years, at the end of which period an electrocardiogram was taken, and it showed right bundle branch block. Clark [7] described three children with complete heart block which

The Research Fund of the Willard Parker Hospital, New York, kindly provided for the use of the electrocardiographic equipment.

1. Lyon, E.: Myocarditis in Virus Diseases of Man, M. Rec. **160**:403, 1947.

2. Saphir, O.: Virus Myocarditis, Mod. Concepts Cardiovas. Dis. **18**:43, 1949.

3. Degen, J. A., Jr.: Visceral Pathology in Measles: Clinico-Pathologic Study of 100 Fatal Cases, Am. J. M. Sc. **194**:104, 1937.

4. Hecht, A. F.: Die Unterscheidung des funktionellen und des organischen Herzblocks, Ztschr. Kinderh. **4**:546, 1912; Das Morgagni-Adams-Stokes'sche Syndrom im Kindesalter und seine Behandlung, Wien. med. Wchnschr. **64**:177, 1914.

5. Neubauer, C.: Myocarditis in Acute Infective Diseases: Review of 200 Cases, Arch. Dis. Childhood **19**:178, 1944.

6. Lyon, E.: Right Bundle Branch Block (Wilson) Following Measles, Acta med. orient. **5**:400, 1946.

7. Clark, N. S.: Complete Heart Block in Children: Report of 3 Cases Possibly Attributable to Measles, Arch. Dis. Childhood **23**:156, 1948.

may have developed while they had measles. However, he felt that "rheumatic carditis and some familial weakness of the conducting tissues may have played a part in the etiology of two of the cases. . . ."

Giustra and Nilsson [8] recently reported the case of a 5½-year-old boy who showed ventricular tachycardia (or supraventricular tachycardia with bundle branch block) on an electrocardiogram recorded 13 days after the onset of measles. Tracings taken on different occasions during the subsequent half year revealed shortened and prolonged P-R intervals and left and right bundle branch block. Fine, Brainerd, and Sokolow [9] found that two patients in a group of eight with measles had "borderline" electrocardiograms.

The question arose of whether abnormal cardiac findings in measles are actually as infrequent as the paucity of reports suggests, or whether disturbances, perhaps of a lesser degree, occur more commonly and could be detected if electrocardiograms of patients with measles were taken routinely. An opportunity to make such a study presented itself in a contagious disease hospital.

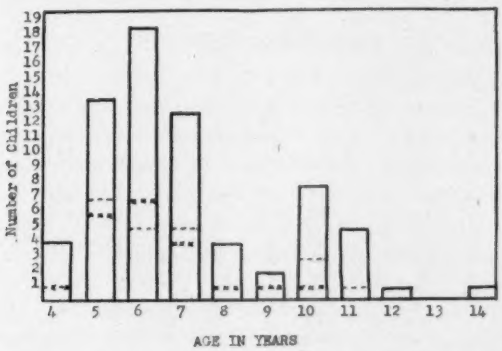

Chart 1.—Age distribution of all children studied (total bar), of children with prolonged P-R intervals (line of crosses), and of children with an R′ wave in lead CF_2 (broken line).

PATIENTS STUDIED

Seventy-one children with measles who were admitted to Willard Parker Hospital between February and June, 1950, were studied. Their ages ranged from 4 to 14 years and were distributed as shown in Chart 1. Sixty per cent of the children were boys. None of the children had had any previous cardiac disease, rheumatic fever, or diphtheria so far as was known, but the histories available were not always complete. The children were free of complications which could be detected clinically, except for two children who had measles encephalitis. All the children survived. At the time of the observations, 29 children were receiving acetylsalicylic acid, 13 penicillin prophylactically, one aureomycin prophylactically, four terpin hydrate elixir, two vasoconstrictor nose drops, and two an antihistaminic preparation. Many children were given a multivitamin preparation. The two patients with encephalitis received barbiturates.

Most of the observations were made while the children were hospitalized. Reexamination could be done on only seven of them after their discharge.

8. Giustra, F. X., and Nilsson, D. C.: Myocarditis Following Measles: Report of a Case, Am. J. Dis. Child. **79**:487 (March) 1950.

9. Fine, I.; Brainerd, H., and Sokolow, M.: Myocarditis in Acute Infectious Diseases: A Clinical and Electrocardiographic Study, Circulation **2**:859, 1950.

METHOD

One hundred five electrocardiograms were photographically recorded with a Sanborn Instomatic Cardiette. A minimum of a 6-in. (15-cm.) strip of each of the standard leads and of precordial leads CF_2, CF_4, and CF_5 was taken. (The precordial series was incomplete in six instances.) The timing device was checked frequently.

The electrocardiograms were taken with the children lying flat on their backs in their own hospital beds, as relaxed physically and mentally as possible. Mental serenity was difficult to obtain because of the youthfulness of the patients, their lack of familiarity with the equipment, and the frequent presence of a language barrier. Most of the records were taken between the time of the afternoon nap and supper. Usually no food had been eaten during the preceding two and one-half hours; however, some of the children had had 4 oz. (118 cc.) of cool fluid orally from a few minutes to two hours before the electrocardiogram was recorded.

The rectal temperatures of the febrile patients were measured within two hours of the time of taking the electrocardiograms; those of the afebrile children were determined twice a day,

TABLE 1.—*Normal Electrocardiographic Values for Children*

		Leads														
		Standard						Precordial								
		I		II		III		2			4			5		
Waves		Mm.	Ref.*	Mm.	Ref.*	Mm.	Ref.*	Mm.	V/CF	Ref.*	Mm.	V/CF	Ref.*	Mm.	V/CF	Ref.*
P	Maximum....	3	L	4	L	3	L	2	CF	K	2	CF	K	2	CF	K
	Minimum.....	0	AH	0.1	L	—1	K	—1	CF	K	—1	CF	K	—1	CF	K
Q	Maximum....	5	L	5	L	8	L	0	CF	A	6	CF	A	4	V	SB
	Minimum.....	0	L	0	L	0	L	0	CF	A	0	V	V	0	V	SB
R	Maximum....	22	L	32	L	25	L	23	V	V	38†	V	V	35‡	V	Y
		..	..	..	..	..	..	..	....	..	28§	V	Y	28§	V	Y
		..	..	..	..	..	..	..	....	..	..	....	..	28‖	V	Y
	Minimum.....	1.5	V	4.3	V	1	K	1	CF	A	1	CF	A	1	CF	K
S	Maximum....	6	L	7	L	6	K	38	V	V	28†	V	V	15‡	V	Y
		..	..	..	..	9¶	SB	..	....	..	18¶	V	SB	12‖	V	Y
		..	..	..	..	..	..	..	....	..	..	....	..	8§	V	Y
	Minimum.....	0	L	0	L	0	L	5	V	SB	0	CF	AH	0	V	SB
T	Maximum....	6	L	8	AH	6	K	10	CF	K	12	V	SB	11	V	V
	Minimum.....	0.2†	V	1	L	—5	K	—8	CF	A	—5	CF	K	0	CF	K
		1.5¶	SB	..	..	..	..	..	....	..	..	....	..	..	....	..
S-T	Maximum....	2	K	2	K	2	K	2.5	CF	K	2	CF	K	2	CF	K
	Minimum.....	—0.5	K	—0.5	K	—0.5	K	—1	CF	K	0	CF	K	—0.5	CF	K
QRS‡	Maximum....	0.09	K	0.09	K	0.09	K	0.10	CF	K	0.10	CF	K	0.10	CF	K
		0.10**	L	0.10**	L	0.10**	L	..	....	..	..	....	..	..	....	..

* Key for references: A, Ash [14a]; AH, Ashman and Hull [13]; K, Katz [14b]; L, Lepeschkin, E.: Das Elektrokardiogramm: Ein Handbuch für Theorie und Praxis, Dresden, Germany, Theodor Steinkopff, 1942; SB, Switzer, J. L., and Besoain, M.: Am. J. Dis. Child. 79:449 (March) 1950; V, Vaquero, M.; Limon Lason, R., and Limon Lason A.: Arch. Inst. cardiol. México 17:155, 1947; Y, Yu, Joos, and Katsampes.[16]

† 0-10 yr. old.
‡ 5-7 yr. old.
§ 11-14 yr. old.
‖ 8-10 yr. old.
¶ 11-15 yr. old.
‡ Figures for QRS are for seconds.
** 10-12 yr. old.

usually not near the time the tracing was recorded. In this series children with temperatures of 100 F. or higher were classified as febrile.

Physical examination of each child's heart was performed immediately after his electrocardiogram was taken.

Since there is a lack of complete agreement about the range of normal values of the various components of the electrocardiogram in children, the values which have been used as standards of normality in this study are presented in Table 1. The figure listed for the minimum amplitude for each wave is the lowest given in any of several reports dealing with normal children's electrocardiograms. Similarly, the values for the maximum amplitudes of the waves and the maximum duration of the QRS complex are the highest recorded in the data consulted. The reference source for each figure is given. Information about the CF precordial leads does not appear to be complete; therefore, values for the corresponding V leads were substituted where indicated in Table 1.

The amplitude and contour of the waves of each lead were observed, and the duration of the QRS complex and the P-R interval was measured in every record. The procedure used in determining the length of the P-R interval in a given electrocardiogram was as follows: Of the standard leads which showed a Q wave, the lead with the highest P wave was used for measuring the P-R (actually P-Q) interval; the longest interval in such a lead was recorded.

A number of methods have been suggested for measuring the duration of electrical systole (Q-T), and also for correcting the Q-T interval for cardiac rate, i. e. calculating the K or Q-T_c. The methods followed in the present work resembled most closely those used by Taran and Szilagyi.[10] The routine electrocardiograms taken in this study did not, however, permit the accurate measurement of as many Q-T intervals (12) in each lead as those investigators measured. In the present series of tracings the Q-T intervals of at least three (and usually more) cycles were measured in each of a minimum of four leads. The R-R intervals of the same cycles were also measured. Measurements were limited to those electrocardiograms in which there were regular rhythms, and in which the ends of the T waves could be clearly determined with a magnifying glass. Only 45 records (43% of those taken) satisfied these criteria.

Bazett's[11] formula, as modified by Taran and Szilagyi,[10] $Q\text{-}T_c = Q\text{-}T / \sqrt{R\text{-}R}$, was used to compute the Q-T_c of each electrocardiogram. The average duration of the Q-T interval in each of the leads in which it had been measured was calculated; the arithmetical mean of these figures was in turn computed and introduced into the above formula as the value for the Q-T. The R-R value (cycle length) used in the formula was obtained in a similar manner.

CLINICAL OBSERVATIONS

A systolic murmur was heard at the third or fourth intercostal space along the left sternal border, or near the apex, on at least one examination in 34 (48%) of the children. These murmurs were interpreted as functional. No diastolic murmur was heard. None of the children presented clinical evidence of endocarditis or of pericarditis.

Certain clinical signs have been accepted as diagnostic criteria of myocarditis. Gallop rhythm has been considered an important one. No instance of it was found in this group. Diminished intensity of or poor quality of the apical first heart sound, which was found to be "the most reliable clinical sign of myocarditis" by Fine and co-workers,[9] was noted in 16 children at the time their electrocardiograms were taken. Nine of these records showed a prolonged P-R interval, which Levine and Harvey[12] consider responsible for "diminution in intensity of the first heart sound" in the presence of a second sound of normal intensity. A metronomic rhythm, another sign suggestive of carditis, was present in two children. It is interesting that 83% of the records taken of children with a soft or poor first heart sound (with a second sound of normal intensity) or a metronomic (tic-toc) rhythm had an R′ wave in lead CF_2 and/or a prolonged P-R interval.

During the course of these observations other symptoms and clinical signs of myocarditis, such as easy fatigability, congestive heart failure, and cardiac insufficiency, were not noted. It could not be said from these observations whether the blood pressure was affected, because it was not routinely determined.

It appears, therefore, that these children presented little clinical evidence of heart disease.

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10. Taran, L. M., and Szilagyi, N.: Duration of the Electrical Systole (Q-T) in Acute Rheumatic Carditis in Children, Am. Heart J. **33**:14, 1947.

11. Bazett, H. C.: Analysis of the Time-Relations of Electrocardiograms, Heart **7**:353, 1920.

12. Levine, S. A., and Harvey, W. P.: Clinical Auscultation of the Heart, Philadelphia, W. B. Saunders Company, 1950.

ELECTROCARDIOGRAPHIC OBSERVATIONS

Rhythm.—The only instance of an abnormal cardiac rhythm was that of a child with ventricular premature contractions. In the rest of the cases studied there was regular sinus rhythm, sinus arrhythmia, or sinus tachycardia.

Conduction Disturbances.—Disturbances in auriculoventricular conduction were found. Thirty per cent of the children had P-R intervals which were longer than the normal values given by Ashman and Hull [13] for the ages and cardiac rates of the respective children. Of these 21 patients, 10 showed the same finding on

TABLE 2.—*Electrocardiograms with Prolonged P-R Intervals* *

Patient	Age, Yr.	Temperature	Cardiac Rate	P-R Interval, Sec.	Prolongation of P-R Interval, %
D. D.	8	Normal	82	0.172	1
J. R.	7	Normal	92	0.164	2
R. B.	6	Normal	103	0.16	3
B. O.	4	101.2 F.	133	0.14	4
T. E.	5	Normal	106	0.161	4
R. J.	10	Normal	97	0.168	5
I. P.	5	Normal	96	0.163	5
W. H.	6	101.2 F.	117	0.152	5
T. H.	5	102.4 F.	144	0.144	7
A. M.	6	Normal	110	0.156	8
V. R.	6	103.6 F.	140	0.144	8
C. G.	6	104.8 F.	154	0.144	8
M. R.	5	Normal	100	0.168	8
W. R.	7	Normal	86	0.184	8
W. R.	7	103.2 F.	127	0.158	9
J. T.	7	103.2 F.	137	0.152	9
L. F.	6	105.2 F.	141	0.148	9
T. E.	5	Normal	111	0.160	10
S. R.	5	Normal	114	0.163	12
R. J.	10	Normal	80	0.190	12
R. B.	6	Normal	111	0.168	12
D. D.	8	Normal	77	0.19	12
A. I.	6	Normal	118	0.163	12
M. S.	7	102 F.	132	0.160	15
M. S.	7	Normal	117	0.172	15
J. T.	7	Normal	88	0.196	15
T. H.	5	Normal	109	0.172	15
J. S.	5	Normal	86	0.192	16
A. I.	6	Normal	89	0.190	21
T. H.	5	Normal	103	0.188	21
S. R.	5	100.2 F.	111	0.20	29
C. G.	9	Normal	95	0.264	55

* According to the standards of Ashman and Hull.

records taken from one day to four months after the original tracings; in four it disappeared within four days.

Since the maximum value which can be considered normal for the P-R interval in children is not universally agreed upon, information about those records in which it is prolonged by the standards of Ashman and Hull has been presented in detail in Table 2. The percentage by which each observed value exceeded the upper limit of normal cited by Ashman and Hull has been included in the table.

The delay in conduction did not seem to be related to the presence of fever, as 26% of the electrocardiograms recorded in febrile children and 33% of the records

13. Ashman, R., and Hull, E.: Essentials of Electrocardiography for the Student and Practitioner of Medicine, Ed. 2, New York, The Macmillan Company, 1941.

of children with normal temperatures had prolonged P-R intervals. The frequency of prolongation of the P-R interval in the younger children was more than twice that in the patients 8 years of age and older. Chart 1 demonstrates the incidence of prolonged P-R intervals at each year of age.

One 7-year-old boy had a complete right bundle branch block, and this was still present six weeks later. There was an R′ wave in lead CF_2 in both of his electrocardiograms, but these two records have been excluded from the subsequent discussion and analysis of this wave.

Changes in Configuration.—The P wave did not differ materially from the normal either in contour or in amplitude. The amplitude was greater than normal (—2 to +2.6 mm.) in lead CF_2 in 12 records, in CF_4 twice, and in CF_5 once. This finding was associated in each instance with a ventricular rate above 100 a minute. In four of these children subsequent electrocardiograms were recorded after the tachycardia had subsided; the amplitude of the P wave had returned to normal.

The QRS complex was of abnormal amplitude in a small number of instances. There was a low R wave in lead I in two records and in lead CF_2 in one tracing. Two electrocardiograms showed a shallow S wave in CF_2. There were four tracings of lead CF_5 in which the S wave had a greater amplitude than the normal value. One child had a Q wave 1 mm. deep in lead CF_2 in two records taken five days apart; this is considered definitely abnormal.[14]

The presence of an R′ wave in leads from the right side of the precordium in children has been described in relatively few published reports. Ash [14a] studied the electrocardiograms of 147 children and found triphasic QRS complexes in right precordial (CF) lead tracings in 15 children, six of whom were ill with rheumatic fever, two with hemorrhagic nephritis, and one with virus pneumonia, and four of whom had congenital heart disease. Three of the latter had an interauricular septal defect, which is often associated with the presence of an R′ wave in lead V_1.[15] Yu, Joos, and Katsampes [16] and Richman and Master [17] found that an R′ wave was inscribed in right-sided precordial (V) leads in a small percentage of normal children.

Although the presence of an R′ wave in right-sided precordial leads may not be abnormal in children, the incidence of its occurrence in those with measles is much higher than in the other groups of children in whom it has been reported. Therefore, the following observations on this wave are presented.

Thirty-one per cent of the children in the present series showed an R′ wave in lead CF_2. In two children it was transitory, subsiding within four days. In six the wave was present in a second electrocardiogram; the longest interval of time between records in this group was 20 days. The amplitudes of the R′ waves were

14. (*a*) Ash, R.: Precordial Leads in Childhood: Comment on the Presence of Double Upward Deflections in Leads from the Sternal Region of Normal Children, Am. J. Dis. Child. **70**:277 (Nov.-Dec.) 1945. (*b*) Katz, L.: Electrocardiography, Including an Atlas of Electrocardiograms, ed. 2, Philadelphia, Lea & Febiger, 1946.

15. Barber, J. M.; Magidson, O., and Wood, P.: Atrial Septal Defect, Brit. Heart J. **12**:277, 1950.

16. Yu, P. N. G.; Joos, H. A., and Katsampes, C. P.: Unipolar Electrocardiogram in Normal Infants and Children, Am. Heart J. **41**:91, 1951.

17. Richman, B., and Master, A. M.: Unipolar Chest and Extremity Lead Electrocardiogram in Children (Newborn to 10 Years Old), Am. Heart J. **41**:687, 1951.

from 1 to 11.4 mm. The R′ wave was smaller than the R wave in 19 of the 29 records. Its height did not depend on the heart rate. There was no evidence of right heart strain in the standard leads.

The average time interval between the start of the QRS complex in lead CF_2 and the peak of the R′ wave was 0.061 second, with a range of 0.042 to 0.076 second. In six of the records with an R′ wave the duration of the QRS complex in lead CF_2 was 0.08 to 0.10 second. The incidence of QRS complexes lasting 0.08 to 0.10 second in CF_2 among the electrocardiograms with an R′ wave was eight times as great as among the records which did not have an R′ wave. The duration of the QRS complex in leads CF_4 and CF_5 was less than 0.08 second in all the tracings.

It is suggested that the presence of an R′ wave in lead CF_2 may be associated with some minor type of conduction defect, possibly a "focal" intraventricular block, in which there is a wide ventricular complex in only one of the precordial leads.[18]

The percentage of electrocardiograms of children under 8 years of age with an R′ wave was two and one-half as great as the percentage in the records of the children 8 years of age and older. The incidence of this finding at different ages is shown in Chart 1. There was no apparent relationship between its presence and such clinical aspects as the presence or intensity of coughing, the severity of illness, the presence of fever, or the duration of hospitalization.

The S-T segment did not deviate from the base line in any record to an abnormal extent, according to the values given in Table 1, by which criteria an elevation up to 2 mm. is normal in the standard leads. Maroney and Rantz,[19] however, found less than 1 mm. of deviation in the standard leads of electrocardiograms of 335 children between the ages of 4½ and 9 years. In the records of four children under the age of 9 years in the present series (and three over 9) the S-T segment was between 1 and 2 mm. above the base line in at least one standard lead. These children were afebrile, and their heart rates were under 104 a minute. In records of two of them taken 17 days and two months later the S-T segments were less than 1 mm. above the base line.

There were no abnormal T waves in the standard leads.

It is felt by some observers that inverted T waves in lead CF_4 are not abnormal in children. However, the incidence of this finding in the electrocardiograms of the children aged 4 through 7 years with measles (19%) was greater than that (3.8%) found by Kuskin and Brockman[20] in 80 normal healthy children of these ages. In lead CF_2 there was also a higher frequency of inverted T waves in the patients (of all ages) with measles than in Kuskin and Brockman's corresponding normal children. In lead CF_5 an inverted T wave was present in the tracings of two children—one 4 years old and one 5 years old. In the series of Kuskin and Brockman inverted T waves in CF_5 were not found in children this old.

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18. Weinberg, H. B., and Katz, L. N.: Two Unusual Types of Electrocardiograms, Am. Heart J. **19**:519, 1940.

19. Maroney, M., and Rantz, L. A.: Electrocardiogram in 679 Healthy Infants and Children, Pediatrics **5**:396, 1950.

20. Kuskin, L., and Brockman, L.: Direction of the Precordial T Wave in 321 Normal Infants and Children, Am. J. M. Sc. **218**:65, 1949.

Electrical Systole.—The values for the Q-T_e varied between 0.390 and 0.454, with an average of 0.425. The distribution of the values is shown in Chart 2.

In studying normal children, Taran and Szilagyi found that 0.405 was the upper limit of normal under optimal conditions of recording an electrocardiogram. They observed that a Q-T_e from 0.406 through 0.430 may be found in normal children during exertion or excitement.[21] Twenty-nine per cent of the Q-T_e values which

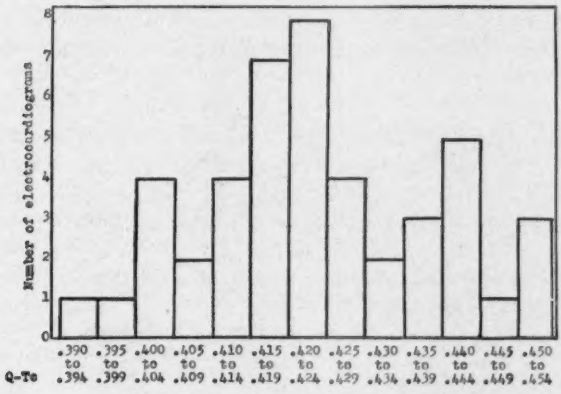

Chart 2.—Q-T_e values of 45 electrocardiograms.

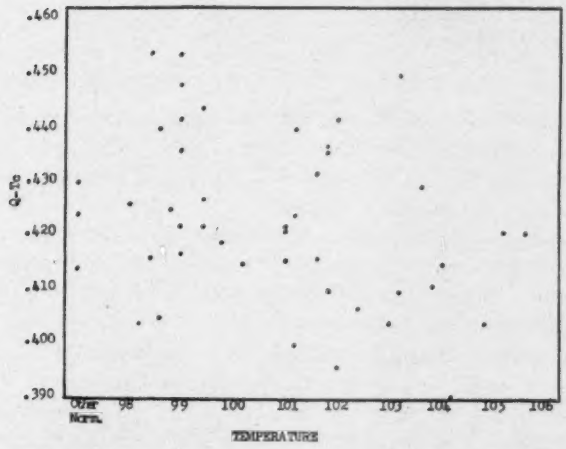

Chart 3.—Temperature and Q-T_e of children with measles.

were determined for the children with measles were above 0.430 and therefore are considered significantly elevated. However, if one accepts 0.405 as the upper value for normal, 87% of the Q-T_e values were above normal.

No significant differences in clinical course could be observed between the group of children with Q-T_e values below 0.430 and the group with higher Q-T_e values. The severity of illness, the presence of cough, the duration of hospitalization, the

21. Taran, L. M., and Szilagyi, N.: Personal communication to the author.

presence of an unusual amount of fear or excitement, and the type of medication received were apparently the same in both groups. From Chart 3 one can see that the Q-T_c was also independent of the patient's temperature.

It has been suggested that abnormalities in conduction possibly invalidate the determination of the Q-T_c.[21] If those electrocardiograms with a prolonged P-R interval or an R′ wave in lead CF_2 are excluded, there remain 23 records in which the Q-T_c was determined; in eight (35%) of these it was above 0.430.

Table 3 summarizes the common electrocardiographic findings which have been discussed. Incidentally, some of the records had more than one of the findings cited.

COMMENT

It is my opinion that in the electrocardiograms recorded in this group of children with measles, the following findings are probably abnormal: complete right bundle branch block, Q-T_c values above 0.430, the high incidence of R′ waves in lead CF_2, and the more markedly prolonged P-R intervals. Although there were

TABLE 3.—*Summary of Electrocardiographic Findings*

	Entire Series		Children Under 8 Yr.		Children 8 Yr. or Older	
	No.	%	No.	%	No.	%
Total number of electrocardiograms	105	..	74	..	31	..
ECG's with a prolonged P-R interval (Ashman and Hull criteria)	32	30	27	37	5	16
ECG's with an R′ wave in lead CF_2	29	28	25	34	4	13
ECG's in which the Q-T_c was determined	45	..	..	..	..	..
ECG's with Q-T_c above 0.430	13	29	..	..	..	..
ECG's with Q-T_c above 0.405	39	87	..	..	..	..

no electrocardiographic records of these children prior to illness, it is presumed that the disturbances developed during the course of their disease.

Prolonged P-R intervals and inversion of T waves have been observed in other acute illnesses.[22] However, the high incidence of R′ waves in lead CF_2 noted in this series of records has not been previously stressed. This may in part be due to the fact that chest leads were not included in the early electrocardiographic studies of infectious diseases. It might also be that for some as yet unknown reason, this particular finding occurs more commonly in measles than in other acute illnesses.

Whether the electrocardiographic findings were the result of actual cardiac involvement by the measles virus or by secondary bacterial invaders or were due to noncardiac factors cannot be established from the present study. In myocarditis of diphtheritic or rheumatic etiology, alterations in the conduction mechanism and prolongation of the Q-T interval may occur; consequently, it is possible that these two types of electrocardiographic abnormalities in the records of the children with measles were the result of myocardial involvement. That prolongation of the Q-T_c might be useful "in evaluating myocardial integrity in patients with infectious disease" was proposed by Joos and Yu,[23] who observed Q-T_c prolongation in five of 23 patients

22. Gibson, S.: The Cardiovascular System, in Brennemann's Practice of Pediatrics, Hagerstown, Md., W. F. Prior Company, Inc., 1948, Vol. 3, Chap. 13, P. 29. Lyon.[1]

23. Joos, H. A., and Yu, P. N. G.: Electrocardiographic Observations in Poliomyelitis: Changes of the Q-T Interval in 23 Cases, Am. J. Dis. Child. **80**:22 (July) 1950.

with acute poliomyelitis. Among the noncardiac factors which also can increase the Q-T are hypocalcemia, hypokalemia, and alkalosis; it is not known whether any of them were present in the subjects of this study.

Changes in acid-base balance and in concentrations of electrolytes may also affect other characteristics of the electrocardiogram, as may hyperventilation, food intake, vitamin deficiencies, anoxia, and fever. However, none of these extracardiac factors usually produces all the types of disturbances found here.

The clinical importance to be accorded the electrocardiographic findings observed in this study is difficult to evaluate. Unfortunately, it was not possible to perform serial electrocardiograms to determine the time required for the tracings to return to normal. In the relatively few follow-up examinations which were made, it was found that all the abnormalities did not subside by the time children usually resume full activity after having had measles. Cardiac damage has not been generally believed to follow. Nevertheless, it may be desirable to extend the period of rest after measles, especially for children under 8 years of age, in whom a higher incidence of electrocardiographic disturbances was found than in the older children.

SUMMARY

A study was made of 105 electrocardiographic records of 71 children hospitalized for measles.

The P-R interval was longer than the Ashman and Hull standards in 30% of the electrocardiograms. An R′ wave was recorded in lead CF_2 in 28% of the tracings.

The Q-T_c value was determined in 45 of the electrocardiograms and was significantly prolonged in 29% of them.

The possible significance of these findings has been discussed.

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Dr. Nelly Szilagyi and Dr. Leo M. Taran of St. Francis Sanatorium for Cardiac Children, Roslyn, N. Y., were very helpful with their advice and suggestions during the preparation of this material.

CRITERIA FOR SANATORIUM CARE OF CHILDREN WITH TUBERCULOSIS

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THE SUSPICION that a child may have tuberculosis usually causes great alarm in the minds of the parents and the physician. Hysteria on the part of the parents and a desire to shift the responsibility on the part of the physician frequently results in the admission to the sanatorium of a child who does not really require sanatorium care. It may follow that the child is unnecessarily exposed to tuberculosis, may receive unnecessary therapy, and may occupy a bed which could much better be utilized for some other patient with active disease.

This paper is intended to clarify the criteria for admission to sanatoria of children with tuberculosis and to discuss some of the issues involved. Pediatricians can be of great service in furthering careful consideration of these problems. The criteria set forth are those in use at the Municipal Tuberculosis Sanitarium of Chicago and reflect the difficulties of institutions in large cities. In these cities roughly 10% of children through the age of 14 years have a positive tuberculin reaction. The vast majority of these children have long recovered from their primary tuberculous infection by the time attention is directed to the chest. If, however, symptoms or abnormal roentgenographic findings are noted in one of these children, it becomes of paramount importance to determine whether the child has active disease and requires sanatorium care.

The work-up of such cases is carried out either by the private physician or by an outpatient clinic. It usually includes a history, physical examination, roentgenograms of the chest, tuberculin test, and search for tubercle bacilli by examination of the sputum, gastric contents, or bronchoscopic aspirate. After the work-up is completed, a decision as to the proper disposition of the patient is necessary. It is at this point that difficulties frequently arise. A simple clinical classification and definite criteria for disposition are very helpful and will be discussed below.

CLINICAL CLASSIFICATION

The following classification of the pulmonary lesion in children is used:

Type I. Primary tuberculosis with positive tuberculin reaction and no lesions visible on the roentgenogram of the chest

Type II. Primary tuberculosis with lesions visible on the roentgenogram
- A. Large hilus glands and insignificant parenchymal component (Fig. 1)
- B. Massive hilus glands causing atelectasis (so-called epituberculosis) (Fig. 2)
- C. Large parenchymal component (Fig. 3)

Type III. Progressive primary tuberculosis (Fig. 4)

Type IV. Reinfection tuberculosis (Fig. 5)

From the Municipal Tuberculosis Sanitarium.

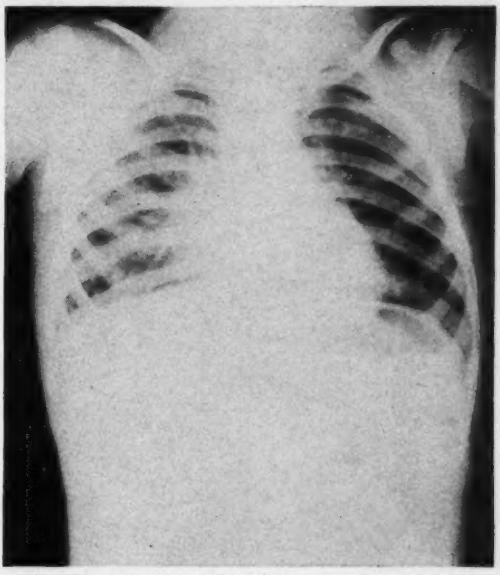

Fig. 1.—Example of Type IIA: Primary tuberculosis with large hilus glands and insignificant parenchymal component.

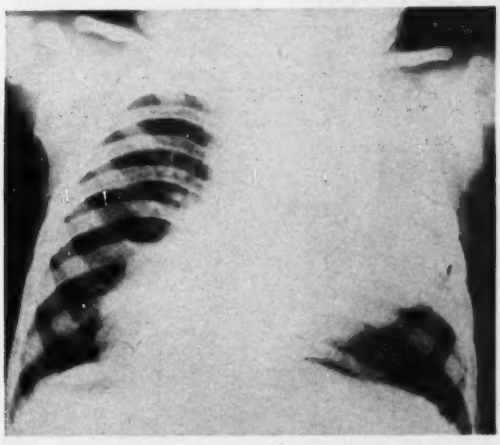

Fig. 2.—Example of Type IIB: Primary tuberculosis with massive hilus glands causing atelectasis, posterior view.

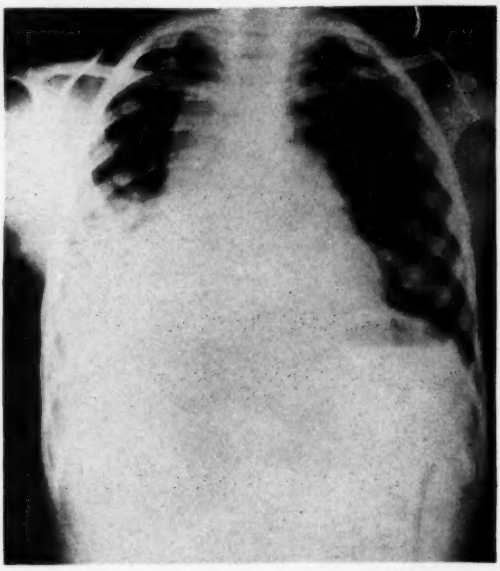

Fig. 3.—Example of Type IIC: Primary tuberculosis with large parenchymal component. There is involvement in the right base with enlargement of right paratracheal glands.

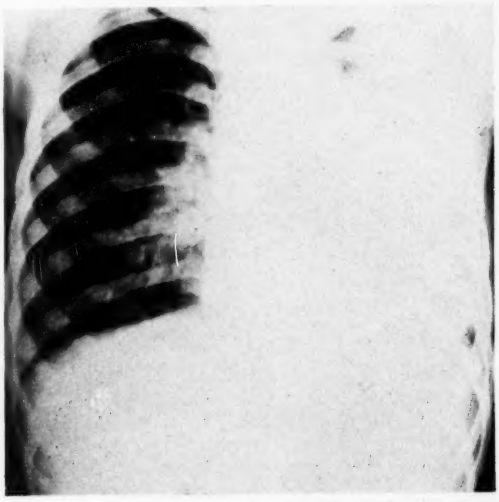

Fig. 4.—Example of Type III: Progressive primary tuberculosis. The primary infection in the left lung, instead of resolving as usual, has spread to involve most of the lung, with apical cavitation.

DIAGNOSIS

Type I: primary tuberculosis with positive tuberculin reaction and normal roentgenogram: The children with this type are usually asymptomatic, although a brief period of fever may occur at the onset of infection. It is important to keep in mind the fact that dissemination of the disease may occur although no primary lesion may be visible on the roentgenogram.

Type IIA: primary infection with large hilus glands shown on the roentgenogram: This group resembles the above except for evidence of enlargement of one or both hilus areas. This may indicate the presence of enlarged lymph nodes. Caffey [1] points out, however, that there is considerable variation in the appearance and size

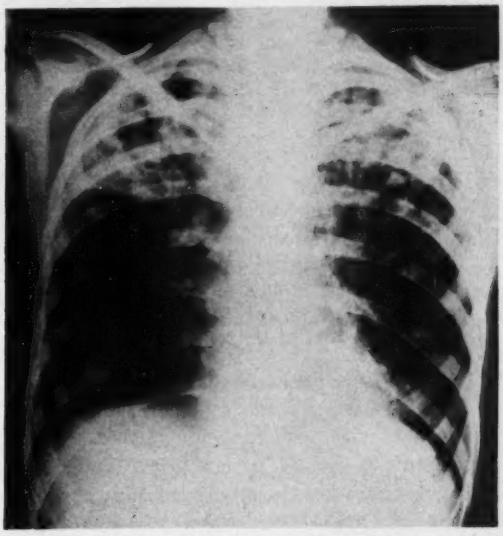

Fig. 5.—Example of Type IV: Reinfection tuberculosis. This child recovered from his primary infection and remained well for several years; then bilateral apical lesions with cavitation, identical with adult phthisis, developed (child 12 years old).

of the hilus in children, so that it is unsafe to conclude that enlargement is glandular. It may be vascular. Lateral roentgenograms are helpful.

Type IIB: primary infection with massive glands causing atelectasis: In addition to the above findings, the roentgenogram shows evidence of atelectasis of a portion of the lung, usually with displacement of the trachea, heart, and diaphragm toward the lesion. Wheezing may be noted on physical examination.

Type IIC: primary infection with large parenchymal component: Symptoms are usually absent or mild, and physical examination reveals little of significance. The roentgenogram shows a parenchymal lesion with hilus involvement on the same side. The parenchymal involvement can be of any size, but occasionally it may involve a considerable portion of the lung.

1. Caffey, J.: Pediatric X-Ray Diagnosis: A Textbook for Students and Practitioners of Pediatrics, Surgery & Radiology, ed. 2, Chicago, The Year Book Publishers, Inc., 1950.

In all the above forms of primary tuberculosis the diagnosis is helped if a knowledge of the time of conversion of the tuberculin reaction is at hand. If conversion was recent, it is axiomatic that the primary focus is still active. The primary focus, according to Wallgren,[2] usually begins to resolve about six months after the onset. However, resolution may be delayed for one to two years. The child may remain asymptomatic in spite of a large parenchymal component, and healing frequently occurs in the absence of any treatment. Cultures of material from the gastric lavage or bronchoscopic aspirate will generally be positive for tubercle bacilli in about 25% of the children with primary tuberculosis.

Type III: progressive primary tuberculosis: In the National Tuberculosis Association's "Diagnostic Standards and Classification of Tuberculosis," 1950 Edition, it is stated:

> Of all persons who acquire primary infection at some time, only a minority develop clinical disease. In some cases, however, the primary infection may be progressive from the beginning (progressive primary) or it may not heal completely and may lie dormant for a time, only to progress later (exacerbation of primary tuberculosis).

Thus, progressive primary tuberculosis results if the primary complex fails to resolve, but instead goes on to cause clinical disease with destruction of pulmonary tissue. The symptoms may vary from mild to severe. On physical examination abnormal pulmonary findings are usually noted. Serial roentgenograms reveal failure of the primary lesion to resolve and progression to destructive lesions with cavitation. Tubercle bacilli can almost always be demonstrated by culture of sputum or gastric lavage material.

Type IV: reinfection tuberculosis: Clinical tuberculosis in children may occur some months or years after apparent healing of the primary lesion. This is identical with phthisis in the adult. The symptoms may be mild to severe. Physical examination usually reveals abnormal pulmonary findings. Tubercle bacilli are usually present in the culture of sputum or gastric lavage material. Roentgenographic examination reveals pulmonary lesions, usually apical, frequently going on to cavitation. The end-result of Type III and Type IV cases is essentially the same: clinical disease with destructive pulmonary lesions.

Dissemination may occur in any of the above forms of tuberculosis, resulting in miliary tuberculosis, tuberculous meningitis, or involvement of other organs. Unfortunately, it is impossible to foretell in which cases disseminated disease will develop. The diagnosis of dissemination is possible only when symptoms and signs have become manifest.

PATIENTS DEFINITELY REQUIRING SANATORIUM CARE

Sanatorium care should imply that the patient requires treatment which cannot be given adequately at home. This includes antimicrobial therapy, collapse therapy, and surgery, with all the necessary adjuvant procedures. On the other hand, those patients who do not require these procedures can be left at home, with outpatient observation.

All will agree that children with evidence of dissemination or with evidence of destructive pulmonary disease, of either the progressive primary or the reinfection

2. Wallgren, A., and Wegelius, C.: Regression of the Hilar Density in Primary Tuberculosis, Acta tuberc. scandinav. **23**:220, 1949.

type, deserve sanatorium care. Early diagnosis and treatment are necessary if good results are to be obtained. Beds should be available for these children at once upon discovery of their disease.

Children with primary infection with massive glands causing atelectasis deserve sanatorium care and treatment. Antimicrobial therapy is indicated, and bronchoscopic aspiration may be helpful.

PATIENTS WHO DO NOT REQUIRE SANATORIUM CARE

It is generally agreed that children with primary tuberculosis as indicated by a positive tuberculin reaction without other abnormal findings do not require sanatorium care.

We believe also that sanatorium care is not indicated for those children with ordinary primary tuberculosis (Types I, IIA, and IIC) who show enlarged glands with or without a parenchymal lesion unless the latter is massive. In support of this concept, we wish to refer to the findings of other workers.

Myers,[3] at the Lymanhurst School for Tuberculous Children, studied three groups of children with primary tuberculosis: (1) those who went to sanatoriums, (2) those admitted to a special school, and (3) those who remained at home with no treatment. He states, "Among these children we were unable to see any difference in the course of the disease regardless of whether the children were treated as strict bed patients, attended a special school, or remained active in the home." In another place he states:

> The first infection type of tuberculosis is an extremely benign disease. After it is fully developed it pursues a retrogressive course no matter how much or how little present day treatment is administered. In rare cases when a physician is called during the febrile stage the individual should be treated just as when fever is caused by any other infection such as influenza. The disease is noncontagious (except in the occasional case with co-existing acute bronchitis) and the symptoms are present over such a short time that the treatment can be carried out in the home. Special forms of treatment such as collapse therapy are of no value and may do harm.

Levine,[4] who studied a group of children in New York, states in his conclusions:

> There was no evidence that rest in bed influenced in any way the course of the primary complex or reduced the incidence of complications and no evidence that lack of rest in bed was in any way detrimental. It would appear that the age of the child at the time of infection rather than the method of treatment was the important factor in determining prognosis. . . . In my opinion, rest in bed during a primary infection with tuberculosis should be limited only to the period of elevation of temperature, as would be advised in the treatment of any febrile condition during childhood.

Painter [5] states: "A more critical evaluation of patients with a primary infection seems indicated with respect to long term hospitalization." He advises that admission should be limited to children who satisfy the following criteria: (1) intimate exposure, (2) acid-fast bacilli found repeatedly, (3) illness and fever, (4) progression of the lesion on roentgenograms, and (5) tuberculous complications.

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3. Myers, J. A., and McKinlay, C. A., editors: The Chest and the Heart, Springfield, Ill., Charles C Thomas, Publisher, 1948.

4. Levine, M. I.: Primary Tuberculosis: Effect of Unrestricted Activity on Prognosis. Am. J. Dis. Child. **68**:385 (Dec.) 1944.

5. Painter, S. L.: Tuberculosis in Children, Dis. Chest **15**:329 (March) 1949.

Biggs [6] reported on a five- to eight-year follow-up of 142 children with primary lesions. He states: "Children with the ordinary primary complex need no treatment except removal from the source of infection. It seems impractical and unnecessary to isolate children with ordinary primary infections."

Opposing views have been reported, but we believe that insufficient consideration has been given to the differentiation of management needed for the various types of disease.

ANALYSIS OF CASES OF SANATORIUM

With the above considerations in mind, an analysis of the various types of tuberculosis in children who were in the sanatorium at various periods during the past 21 years was carried out. This revealed the following facts: From 1930 through 1950 there were 1,749 admissions and 110 deaths. At any one time the children's ward usually had the following proportions of the various types: Type IIA (hilus enlargement alone), about 25%; Type IIC (with large parenchymal lesion), about 25%; Type III and Type IV (destructive pulmonary disease), 30 to 50%. The others were patients with miliary tuberculosis, tuberculous meningitis, atelectasis, or diagnostic problems.

The significant finding is the large percentage of patients with Types IIA and IIC, who could well have remained at home. They usually were admitted when discovered to be in contact with an adult with open disease. They were practically always asymptomatic and revealed no evidence of clinical illness. It was customary to keep them in the sanatorium until three negative gastric cultures were obtained. As a result, they occupied beds for periods ranging from a few months to two years. We now believe that these children unnecessarily occupied beds which could have been put to better usage.

COMMENT

We believe that the evidence indicates that children with Type I, Type IIA, or Type IIC tuberculosis generally do not require sanatorium care. These children can be allowed to remain at home and continue their usual activities, but they should be observed by the physician or outpatient clinic at appropriate intervals. Possible exceptions to this rule are infants under 2 years of age, in whom the danger of dissemination is much greater, and any children who have massive parenchymal involvement. These two groups deserve sanatorium care if beds are available.

Children with Type IIB tuberculosis, with massive glands and atelectasis, require sanatorium care so that they can receive antimicrobial therapy and bronchoscopic aspiration as indicated.

Children with Type III and Type IV, with destructive tuberculosis, require sanatorium care as soon as possible. Although children do not cough much, these groups often have heavily positive sputum, and if possible they should be separated from the children who have primary disease, those with Types I and II.

Children with evidence of disseminated disease, including miliary tuberculosis and tuberculous meningitis, should be considered emergencies for immediate hospitalization.

In order to simplify the consideration of new patients seen at our outpatient clinics, we have furnished the clinics with an outline of the above criteria. The list

6. Biggs, A. D.: Primary Complex of Pulmonary Tuberculosis, Am. J. Dis. Child. **80**:566 (Oct.) 1950.

indicates roughly the priority of each group as to urgency of hospital care. Group C allows for individual consideration of exceptional patients who do not fit into the usual classification.

The exceptional patients who require individual consideration usually are those who have Type IIB tuberculosis and those for whom it is difficult to state whether the parenchymal lesion is likely to resolve or may be going on to progressive clinical disease. The former group, as indicated above, should be hospitalized. In the latter group each patient requires separate consideration. If asymptomatic, they can be observed for a few months. In cases in which there is doubt, probably the patient should be hospitalized and given treatment.

RELATED PROBLEMS

Are Children with Positive Gastric Cultures Infectious?—Children with primary tuberculosis, Types I and II, have tubercle bacilli which can be demonstrated in the gastric contents in about 25% of the patients, according to Wallgren. The possibility that such children can spread the disease seems to be a controversial question. In some places such children are isolated; in other places they are ignored. Myers, as noted above, states that such children are noncontagious.

Criteria for Sanatorium Care of Children with Tuberculosis

A. The following types of cases definitely require sanatorium care:
   1. Miliary tuberculosis.
   2. Tuberculous meningitis.
   3. The adult type (destructive type) of tuberculosis. X-rays should usually reveal evidence of cavitation. Tubercle bacilli should be demonstrated by positive sputum, stomach wash culture, bronchoscopic aspirate culture or guinea pig inoculation.
   4. Progressive primary tuberculosis with tubercle bacilli demonstrated as above. In order to be classified as a progressive primary lesion there should be x-ray evidence of parenchymal inflammatory disease which has failed to resolve after several months of observation.

B. The following types of cases do not require sanatorium care:
   1. Primary tuberculosis as indicated by a positive Mantoux test with evidence of enlarged glands in the mediastinum or elsewhere, but without parenchymal disease.
   2. Primary tuberculosis as evidenced by a positive Mantoux test, plus a parenchymal pulmonary lesion of less than four months' duration.

C. Exceptional cases: Cases that do not fall definitely within one of the above classifications may be considered on their individual merits.

Jensen and Bindslev,[7] discussing possible infection from patients with bacilli in the gastric contents, state:

> Even though this possibility cannot be excluded with absolute certainty, however, our investigations suggest that from an epidemiological point of view, in comparison with bacillary phthisics, the risk of infection from such patients merely amounts to a drop in the ocean. This applies in particular to the children who invariably swallow their sputum and thus deposit no infectious material in handkerchiefs or other places—something that seems to be of importance to the risk of infection involved.

Since thousands of children in a large city pass through their primary tuberculous infection, and since there has been no good evidence adduced to indicate that they spread disease, it appears to us that the danger from this source is negligible. We believe, therefore, that such children should be considered noncontagious and should not be kept home from school nor placed in a sanatorium for this reason alone.

7. Jensen, K. A., and Bindslev, J.: Studies on the Virulence and Germinating Percentage of Tubercle Bacilli in Sputum, Acta tuberc. scandinav. **20**:65, 1946.

Observation Wards.—In a considerable number of children it may be difficult to distinguish quickly between tuberculosis and other diseases. The diagnosis often awaits bacteriological confirmation by culture or guinea pig inoculation, yet some of the children may be clinically ill and require hospital care. To place such children in a tuberculosis sanatorium for observation may expose them to the possibility of tuberculous infection. It would be far more satisfactory if observation wards could be set up in general hospitals. Appropriate measures for the isolation of each patient are necessary. It is preferable that children should not be admitted to a tuberculosis institution until a definite diagnosis of tuberculosis has been verified.

Should Children with Primary Lesions Receive Streptomycin Therapy?—It has been proposed that treatment with streptomycin early in the course of the primary disease may prevent or minimize the dissemination of tubercle bacilli to various organs in the body, as postulated by Ranke. It might also favor quicker and more complete healing of the primary complex. On the other hand, there is the danger that the patient thereafter would harbor resistant organisms, with the result that treatment of a future exacerbation would be difficult. This problem has brought out a sharp division of opinion. It is self-evident that the vast majority of children with primary tuberculosis recover without any difficulty. Treatment early in the course of the primary disease is usually impractical because the disease is generally discovered months or years after the onset. In those children in whom the time of conversion of tuberculin reaction is known to be recent, treatment could be considered. We feel that it may be indicated particularly in infants, especially those who are nonwhite, since the percentage of dissemination is much greater at this age and in this group.

SUMMARY

Criteria are offered to effect a logical separation of children who require sanatorium care for tuberculosis from those who do not. It is contended that a considerable number of children are unnecessarily placed in sanatoria, resulting in possible exposure, excessive therapy, and waste of valuable bed space. Some of the related problems are discussed, including the alleged danger of infection from children with tubercle bacilli in the gastric contents and the question of streptomycin therapy in primary tuberculosis.

RENAL FUNCTION STUDIES IN PEDIATRICS

II. Influence of Magnesium Sulfate on Renal Hemodynamics in Normal Children

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COMPLICATIONS of acute hemorrhagic nephritis, such as hypertension, cardiac failure, encephalopathy, oliguria, and anuria, can usually be traced directly or indirectly to generalized arteriolar spasm. Since the observation was reported by Blackfan and McKhann [1] and Blackfan and Hamilton [2] that magnesium sulfate is effective in relieving hypertension, this compound has been widely used in the treatment of hypertension in nephritis. Our present knowledge of the action of parenterally administered magnesium salts has been excellently reviewed by Smith, Winkler, and Hoff,[3] who present an extensive bibliography of the subject. They reported a correlation between the action of magnesium on various organ systems with serum magnesium levels. They have also pointed out that cardiovascular effects may be produced by relatively small increments in serum magnesium levels and that further increments result in respiratory depression and other severe toxic manifestations. Stanbury [4] has shown the blocking action of magnesium on sympathetic ganglia, and Rubin and Rapoport [5] have concluded that the beneficial effects of magnesium in the treatment of hypertension associated with nephritis are probably attributable to generalized relaxation of arterioles due to direct action

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From the Division of Pediatrics, University of Tennessee College of Medicine, and the Department of Pediatrics of the John Gaston Hospital.

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1. Blackfan, K. D., and McKhann, C. F.: Acute Glomerular Nephritis in Children: Treatment of Cerebral Manifestations, J. A. M. A. **97**:1052 (Oct. 10) 1931.

2. Blackfan, K. D., and Hamilton, B.: Uremia in Acute Glomerular Nephritis: Cause and Treatment in Children, Boston M. & S. J. **193**:617, 1925.

3. Smith, P. K.; Winkler, A. W., and Hoff, H. E.: Pharmacological Actions of Parenterally Administered Magnesium Salts: Review, Anesthesiology **3**:323, 1942.

4. Stanbury, J. B.: Blocking Action of Magnesium Ion on Sympathetic Ganglia, J. Pharmacol. & Exper. Therap. **93**:52, 1948.

5. Rubin, M. I., and Rapoport, M.: Mode of Action of Magnesium Sulfate in Reducing Hypertension of Acute Glomerulonephritis, Am. J. M. Sc. **201**:734, 1941.

on smooth muscle rather than to a reduction in edema of the brain. Bernstein and Simkins [6] have tabulated the serum magnesium levels in a variety of clinical states and have observed levels twice that of normal in patients with chronic nephritis. Hirschfelder [7] has emphasized the danger of purgation using magnesium sulfate in patients with renal insufficiency because of the toxic serum levels which may result. McCance and Widdowson [8] have studied the effect of intravenously administered magnesium on normal persons and have observed that the administered magnesium is excreted mainly by way of the kidney.

Since little is known about the effect of magnesium on renal hemodynamics in normal children and in children with acute nephritis, we have undertaken such studies. The following report on normal children may serve to expand our knowledge of the pharmacological action of this drug on the kidneys and may thereby help to establish a more rational basis for its use.

METHODS AND MATERIAL

Fifteen children between the ages of 5 and 11 years without renal disease were admitted to the hospital for study. Glomerular filtration rate (mannitol clearance), effective renal plasma flow (paraaminohippurate [PAH] clearance) and maximal tubular excretory capacity (Tm.) for PAH were measured. Twenty-four to forty-eight hours after control clearances were determined, magnesium sulfate was administered, and repeat clearances were performed on each child. The dose of magnesium sulfate in all instances was 100 mg. per kilogram of body weight (0.2 cc. of a 50% solution) and was administered intramuscularly every four hours for three to four doses prior to the second clearance. Clearances were determined two hours after administration of the last dose of magnesium sulfate. Blood pressure, measured by the conventional cuff method, was followed during the course of magnesium injection as well as during the time that clearances were being performed. Details for determining the clearance values as well as analytical procedures for PAH and mannitol have been described in a previous publication.[9] Serum magnesium levels were determined by a modification of the method of Denis described by Hawk, Oser and Summerson.[10]

RESULTS

Results of magnesium sulfate injection on individual clearances as well as on serum magnesium levels are reported in Table 1, and the percentage of alteration in each measured process and derived value and the critical ratio are shown in Table 2. Statistical analysis involved the determination of the critical ratio for all the data.[11]

During the control clearances the serum magnesium level ranged from 1 to 1.5 mEq. per liter, with an average of 1.15 mEq. After the administration of mag-

6. Bernstein, M., and Simkins, S.: Magnesium Content of the Blood Serum and Urine, J. Lab. & Clin. Med. **26**:521, 1940.

7. Hirschfelder, A. D.: Clinical Manifestations of High and Low Plasma Magnesium: Dangers of Epsom Salt Purgation in Nephritis, J. A. M. A. **102**:1138 (April 7) 1934.

8. McCance, R. A., and Widdowson, E. M.: Fate of Calcium and Magnesium After Intravenous Administration to Normal Persons, Biochem. J. **33**:523, 1939.

9. Etteldorf, J. N.; Tuttle, A. H., and Clayton, G. W.: Renal Function Studies in Pediatrics: I. Renal Hemodynamics in Children with Sickle Cell Anemia, Am. J. Dis. Child., to be published.

10. Hawk, P. B.; Oser, B. L., and Summerson, W. H.: Practical Physiological Chemistry, ed. 12, Philadelphia, The Blakiston Company, 1947, pp. 593 and 594.

11. Critical ratio = mean difference $\div \sqrt{\Sigma d^2/n} \div \sqrt{n}$, in which n is the number of patients and Σd^2 is the sum of the squared deviations of the difference between the values obtained during the control and subsequent clearance in each patient from the mean difference.

nesium sulfate the concentration ranged from 2 to 5 mEq. per liter, with an average of 3.2 mEq. These levels are within the range reported by Smith and his associates [3] as being capable of affecting the cardiovascular system. Because of the pain associated with the injection of magnesium sulfate and the anxiety associated with the

TABLE 1.—*Renal Clearances in Normal Children Before and After Intramuscular Administration of Magnesium Sulfate*

Patient	Sex	Age, Yr.	Surface Area, M.²	GFR, Cc./Min.*		ERPF, Cc./Min.*		TMPAH, Mg./Min.*		GFR × 100/ ERPF †		GFR/ TMPAH		ERPF/ TMPAH		Serum Magnesium, mEq./L.	
				Control	After $MgSO_4$	Control	After $MgSO_4$	Control	After $MgSO_4$	Control	After $MgSO_4$	Control	After $MgSO_4$	Control	After $MgSO_4$	Control	After $MgSO_4$
B. P.	M	10	1.11	113	137	454	519	98	102	24.9	26.4	1.22	1.34	4.9	5.1	1.5	2.0
A. C.	M	10	1.10	133	111	733	739	98	112	18.2	15.0	1.35	0.99	7.5	6.6	1.5	3.0
C. T.	M	9	1.11	111	79	418	473	82	102	26.6	16.7	1.35	0.77	5.1	4.7	...	3.5
W. C.	M	5	0.81	144	121	626	789	95	137	23.0	15.4	1.52	0.89	6.6	5.8	1.0	3.0
D. F.	F	7	0.99	127	119	657	605	101	92	19.3	19.7	1.26	1.29	6.5	6.6	1.0	3.5
C. F.	F	6	0.75	110	104	541	589	66	86	20.4	17.7	1.67	1.21	8.2	6.9	1.0	3.5
J. B.	F	10	1.14	138	152	781	889	89	112	17.7	17.1	1.55	1.35	8.8	7.9	...	2.5
M. P.	F	10	1.12	110	111	559	520	83	84	19.7	21.4	1.33	1.32	6.7	6.2	...	3.0
C. L.	F	11	1.12	154	133	642	724	104	118	24.0	18.4	1.48	1.13	6.2	6.1	1.0	3.5
W. F.	M	9	0.93	175	103	733	645	96	103	23.9	16.0	1.79	1.00	7.5	6.3	...	3.0
N. F.	M	8	0.90	140	121	771	657	94	92	18.2	18.4	1.49	1.32	8.2	7.1	1.0	4.0
J. P.	M	6	0.87	113	99	...	...	89	111	....	....	1.27	0.89	...	...	1.0	5.0
A. W.	M	7	0.97	148	163	784	882	116	126	18.9	18.5	1.27	1.30	6.8	7.0	1.5	3.0
A. T.	M	9	1.02	142	154	516	740	113	131	27.2	20.8	1.25	1.18	4.6	5.7	...	3.0
M. D.	F	5	0.79	104	124	555	591	..	...	18.8	21.0	....	....	...	...	1.0	3.0
			Average	131	122	627	669	94	108	21.5	18.8	1.41	1.14	6.7	6.3	1.15	3.2

* Corrected to 1.73 square meters of surface area.
† Filtration fraction.

TABLE 2.—*Percentage of Change in Renal Functions Following Intramuscular Administration of Magnesium Sulfate to Normal Children*

Patient	GFR	ERPF	TMPAH	GFR × 100 * / ERPF	GFR / TMPAH	ERPF / TMPAH
B. P.	+ 21.1	+ 14.3	+ 9.7	+ 6.0	+ 10.0	+ 4.1
A. C.	− 16.5	+ 0.8	+ 14.2	− 17.6	− 26.6	− 12.0
C. T.	− 28.8	+ 13.1	+ 24.4	− 37.2	− 43.0	− 7.8
W. C.	− 16.0	+ 26.0	+ 44.2	− 33.0	− 41.5	− 12.1
D. F.	− 6.3	− 7.9	− 8.9	+ 2.0	+ 2.4	+ 1.5
C. F.	− 5.5	+ 8.7	+ 30.3	− 10.6	− 27.5	− 15.8
J. B.	+ 10.1	+ 13.8	+ 25.8	− 3.4	− 12.9	− 10.2
M. P.	+ 0.9	− 7.0	+ 1.2	+ 8.6	− 0.7	− 7.5
C. L.	− 13.6	+ 12.8	+ 13.5	− 23.3	− 23.7	− 1.6
W. F.	− 41.0	− 12.0	+ 5.1	− 33.0	− 44.0	− 16.0
N. F.	− 13.5	− 14.8	− 2.1	+ 1.1	− 11.4	− 13.4
J. P.	− 12.4	.....	+ 24.8	.....	− 29.9	.....
A. W.	+ 10.1	+ 12.5	+ 8.6	− 2.1	+ 2.4	+ 2.9
A. T.	+ 8.5	+ 43.5	+ 15.9	− 23.5	− 5.6	+ 14.5
M. D.	+ 19.2	+ 6.5	.....	+ 14.9	.....	.....
Critical ratio	1.29	1.56	4.01	2.15	3.81	2.12

* Filtration fraction.

clearance procedures, blood pressure determinations were considered unreliable; however, we occasionally observed a slight reduction.

The glomerular filtration rate (GFR) during the control studies ranged from 104 to 175 cc. a minute, with an average of 131 cc. After magnesium sulfate administration the GFR was found to be decreased in nine cases, increased in five, and unaltered in one. Values ranged from 79 to 163 cc. a minute, with an average of

122. Although there was a reduction in the average GFR after administration of magnesium sulfate, the critical ratio of 1.29 indicated that magnesium exerted no significant influence on this important renal function.

The effective renal plasma flow (ERPF) during the control periods ranged from 418 to 784 cc. a minute, with an average of 627 cc. After magnesium sulfate administration the ERPF ranged from 473 to 889 cc. a minute, with an average of 669 cc. In nine cases the ERPF was increased; in four cases it was decreased, and in one case it was unaltered. Although the average value showed a slight increase, this was insignificant because the critical ratio was less than 2.0.

The filtration fraction (GFR $\times$ 100/ERPF) during the control period ranged from 17.7 to 27.2%, with an average of 21.5%. After magnesium sulfate administration the filtration fraction ranged from 15 to 26.4%, with an average of 18.8%. This fraction was decreased in seven cases, increased in three cases, and unchanged in four cases after the administration of magnesium sulfate. The average filtration fraction was reduced by the magnesium sulfate; however, this reduction was insignificant, as attested by the critical ratio of 2.15.

The Tm_{PAH} (maximal tubular excretory capacity for PAH) during the control periods ranged from 66 to 116 mg. a minute, with an average of 94 mg. After magnesium sulfate administration the Tm_{PAH} ranged from 84 to 137 mg. a minute, with an average of 108 mg. In 11 of 14 cases it was increased; in 1 case it was reduced, and in 2 cases it was unaltered. The increase in Tm_{PAH} was statistically significant, with a critical ratio of 4.01, and this is the only measured function observed in this study to be significantly altered.

The derived value GFR/Tm_{PAH} was significantly decreased, with a critical ratio of 3.8. Inspection shows that this is obviously due mainly to the increased Tm_{PAH}, although in most instances the GFR tended to be reduced after magnesium sulfate administration.

The derived value $ERPF/Tm_{PAH}$, which indicates perfusion of normal tubular excretory tissue with plasma, was not significantly altered, since the critical ratio was 2.12.

Under the conditions of this study no consistent relationship was observed between the serum magnesium level and any of the measured functions.

COMMENT

From these data it is apparent that in the absence of arteriolar spasm such as is present in hypertension associated with acute nephritis, increasing the serum magnesium concentration to the levels which were attained in these children results in no significant alterations in GFR and ERPF. The Tm_{PAH}, however, is definitely increased in the majority of cases. Magnesium apparently exerts its influence on the tubular portion of the normal nephron by some method other than a hemodynamic one. However, it is interesting to note that the ratio $ERPF/Tm_{PAH}$ was not significantly altered, even though the Tm_{PAH} was increased. The role of magnesium as an enzyme activator [12] may be offered as a possible explanation for the increase in Tm_{PAH}.

12. Sumner, J. B., and Somers, G. F.: Chemistry and Methods of Enzymes, ed. 2, New York, Academic Press, Inc., 1947, pp. 190 ff.

These results are in agreement with those of the incompletely published renal hemodynamic studies of Harris and DeMaria.[13] They observed that an increase in the plasma magnesium concentration in normal children comparable to that produced in patients during the hypertensive phase of acute nephritis did not alter filtration and plasma flow. No Tm_{PAH} values were reported.

SUMMARY

Renal hemodynamic studies have been completed in 15 normal children before and after the intramuscular administration of magnesium sulfate.

Preinjection serum magnesium levels in normal children ranged from 1.0 to 1.5 mEq. per liter, with an average of 1.15 mEq.

After the intramuscular administration of 100 mg. per kilogram of a 50% solution of magnesium sulfate, the serum magnesium levels ranged from 2.0 to 5.0 mEq. per liter, with an average of 3.2 mEq.

GFR tended to decrease after magnesium sulfate administration; however, this was insignificant.

ERPF increased slightly but insignificantly.

The filtration fraction was insignificantly reduced.

The Tm_{PAH} was significantly increased.

The ratio ERPF/Tm_{PAH} was not significantly altered.

The ratio GFR/Tm_{PAH} was significantly reduced.

13. Harris, J. S., and DeMaria, W. J. A.: Effect of Intravenous Magnesium Sulfate on the Renal Dynamics of Acute Nephritis in Childhood, Abstracts, Society for Pediatric Research, 1950, p. 33.

METHOD FOR OBJECTIVE MEASURE OF DEVELOPMENTAL PROGRESS

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THE SLOW grower or child who does not measure up to his chronological age group with respect to one or more aspects of development has during recent years increasingly stimulated the interest of the clinician. From a state of affairs in which these so-called exceptional children were more or less neglected, a shift has taken place: Today, innumerable supportive measures have been introduced to help the physically or otherwise handicapped child to grow and develop.

The habilitation movement has itself suffered some growing pains which stem not only from the practical problems of setting up adequate programs, but also from the difficulties involved in evaluating the child's progress. The outstanding need is for an objective measure which will indicate the extent to which special training or other help has contributed to the child's development.

It seems that this need is beginning to be recognized by workers in the field who themselves are somewhat uncertain as to factors underlying the child's improvement or lack of improvement with treatment. The problem, however, seems twofold. It includes consideration not only of the possible effects of the specific treatment applied but also of growth and development as it usually occurs.

It has been scientifically demonstrated, for example, that there are differences in rates of growth from one child to the next and that there is at the same time continuity in growth. The child's past developmental history is the basis in a large measure for the prediction of his future progress. Again, studies have shown that in a wide variety of functions which depend upon maturational factors, special training has limited value. Best results are achieved when the child is developmentally ready. Again, it has been repeatedly indicated that special methods to stimulate growth have succeeded most effectively in those instances in which there has been deprivation and when the child has the capacity for better functioning.

A realistic approach is by recognition of the fact that although in many instances a good deal can be achieved by special opportunities such as are afforded in current habilitation programs, there is very little that can be done beyond the limitations of the individual child's capacities and rate of growth.

It is not often possible to determine the extent to which environmental factors of a positive or negative nature have played a role of influencing a given child's present developmental status. Consequently, criteria for institution of treatment

From the Cerebral Palsy Preschool Center, Lenox Hill Hospital.

cannot be too well defined. However, once a child has begun receiving treatment of any kind, there should be available a method for objective evaluation of progress made.

The technique presented in this paper seems to have practical value in that it shows where the individual child stands in comparison with average children in his chronological age group. Using as a frame of reference available norms [1] which have been scientifically established, it is possible to indicate graphically specific behaviors present before the onset of treatment as well as those new skills which appear after treatment is initiated.

In addition, the chart indicates the extent to which the behaviors under consideration fall within, or deviate from, what may be expected from the average child.

The time units which are an integral part of the chart furnish a clue as to what extent deviations may possibly be due to environmental deprivation and to what

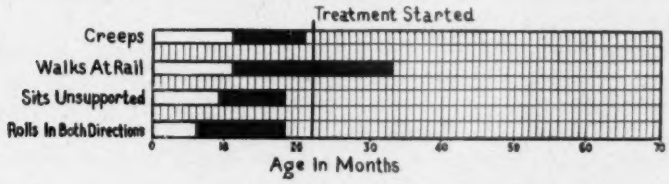

Chart 1.—Developmental progress of Patient A

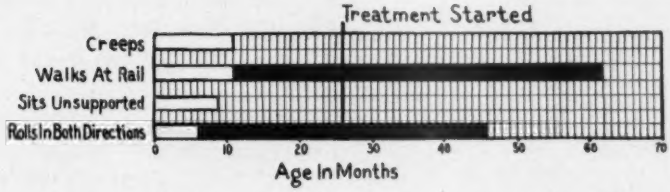

Chart 2.—Developmental progress of Patient B.

extent they may be considered due to the child's lack of potential. To clarify, one might assume that when there is conspicuous improvement after the start of treatment, the child has suffered deprivation and can thus profit from the special stimulation.

Charts 1 and 2 are based on data obtained from treatment records of two children with cerebral palsy.[2] The graphic representations are but sections of the total scale of motor development. Scales for charting both motor and functional development have been assembled.[3]

1. Gesell, A., and Amatruda, C. S.: Developmental Diagnosis: Normal and Abnormal Child Development, Clinical Methods and Pediatric Applications, ed. 2, New York, Paul B. Hoeber, Inc., 1947.

2. The data are taken from records of patients at the Cerebral Palsy Preschool Center, Lenox Hill Hospital, New York. They are presented with permission of Dr. George Deaver, Medical Director.

3. Blum, L. H., and Fieldsteel, A. M.: Cumulative Record of Motor Behavior, Cumulative Record of Functional Behavior, Yonkers, New York, World Book Company, to be published.

The abscissa, or base line, in the charts represents time units in months. Along the ordinate the significant behavior items are listed. The age at which the behavior appears in the average child is indicated by the right end of the outlined bar. The age at which the particular patient has achieved the activity is represented by the right end of the solid bar. Thus, the solid bar indicates the difference between average development and the development of the particular child. The age at which the patient started receiving treatment is marked by the heavy vertical line.

Chart 1 shows the progress made by Patient A. Reading the chart, one can see that the child started receiving therapy when she was 22 months old, at which time she had already achieved the following activities: rolls in both directions, sits unsupported, and creeps. The chart further shows that these activities appeared at 18 months, 18 months, and 21 months respectively; when these figures are compared with the norms of 6, 9, and 11 months, respectively, the considerable lag is evident. To the right of the vertical line it is noted that at the age of 33 months, which is 11 months after the onset of treatment, the patient walks at rail. This activity normally appears at 11 months.

Examination of the record of Patient B shows that the activity rolls in both directions was not achieved until 46 months—20 months after he entered treatment. The record indicates that this patient still has not accomplished the activity sits unsupported. At 62 months he achieved the activity walks at rail. A glance at the chart shows that this child still cannot creep.

The obvious advantage of objective recording in this manner is that it gives one a complete visual picture of the child's history from the point of view of his motor and functional development. It also allows comparison of children who are in similar programs of therapy. For example, Patient A shows more uniformity than Patient B with respect to the emergence of various activities and less of a deviation from so-called normal or average development.

With respect to Patients A and B, the one activity which can be compared is walks at rail. The figures show that it took Patient B two years and one month longer than Patient A to achieve this activity. Discussion of the various influencing factors which might account for the differences in rate of progress of these two children is not within the scope of this paper.

SUMMARY

This paper points out the present unsatisfactory method of using broad descriptive terms such as "making progress" or "improving" with respect to the child-patient receiving treatment. A more scientific approach is an objective evaluation of progress. The paper presents a method of charting the child's rate of progress concurrently with treatment to furnish a basis for determining the extent to which treatment is effective. This method is easy to use and interpret. The technique can be used not only with the motor-handicapped child, as illustrated here, but also in evaluating progress of children with other kinds of retardation and disabilities.

EGG ALLERGY IN CHILDREN

Incidence and Evaluation in Relation to Chick-Embryo-Propagated Vaccines

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EGG IN relation to the problem of food allergy is perhaps too well understood today to warrant more than passing comment. It assumes new interest, however, in its bearing on the increasing use of viral and rickettsial vaccines prepared from chick embryos. Clinical experience with such vaccines indicates that their use may be fraught with danger in those cases in which the patients are sensitive to egg. A study of the incidence and interpretation of egg sensitivity that may be encountered in a random population, as well as in allergic persons, is therefore pertinent.

INCIDENCE OF EGG SENSITIVITY IN NONALLERGIC CHILDREN

Normal persons have been tested with egg proteins to evaluate the significance of skin tests, and the general survey suggests an incidence of egg sensitivity of less than 1% in a random group of infants and children.

Blackfan [1] found no positive reactors among 43 children tested with egg albumin by the scratch method. With intracutaneous tests he encountered one child among 19 who demonstrated a positive reaction. Baker [2] discovered one positive reaction in a group of 25 children. Peshkin and Rost,[3] using the scratch test technique, reported four suggestively positive reactions among 204 children. Moro [4] made scratch tests on 362 infants with egg white and obtained no positive reactions. These investigators, however, excluded all allergic children prior to testing, by ruling out any children with either a history or physical findings suggestive of the major allergic syndromes.

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From the Departments of Pediatrics and Immunology, New York Medical College, Flower and Fifth Avenue Hospitals, and the Pediatric Division of Sea View Hospital.

1. Blackfan, K. D.: Cutaneous Reaction from Proteins in Eczema, Am. J. Dis. Child. **11**:441 (June) 1916.

2. Baker, H. M.: Incidence of Protein Sensitization in the Normal Child, Am. J. Dis. Child **19**:114 (Feb.) 1920.

3. Peshkin, M. M., and Rost, W. L.: Incidence of Protein Sensitization in the Normal Child, Am. J. Dis. Child. **23**:51 (Jan.) 1922.

4. Moro, E.: Ekzema infantum und Dermatitis seborrhoides: Klinik und Pathogenese, Berlin, Springer-Verlag, 1932.

Pearson,[5] using three concentrations of egg proteins intracutaneously, found no reactors with the weak concentrations and extremely few with the stronger ones.

Carr and Ratner,[6] studying 410 infants under 1 year of age, disclosed two positive reactors to egg white. In their study these investigators did not eliminate infants with allergy, and thus this group more closely approximates a random selection in a particular age group. Smyth and Bain [7] failed to find positive dermal reactions to egg in a group of newborn infants studied; however, Balyeat [8] reported one positive reactor to egg in a group of 119 newborn infants.

TABLE 1.—*Survey of Dermal Reactions in Relation to Clinical Sensitivity in a Random Selection of Children Tested Intracutaneously with Egg White and Chicken Feathers*

No. Tested	Case No.	Patient	Age, Yr.	Dermal Reactions To Egg White	Dermal Reactions To Chicken Feathers	Clinical Sensitivity to Egg White and Chicken Feathers
Positive dermal reactors						
10	1	K. K.	8	3+	+	Vomiting, urticaria, angioneurotic edema, asthma, and eczema follow ingestion of uncooked egg
	2	L. W.	5	+	+	Tolerates egg; has had eczema
	3	J. D.	12	+	+	No allergy
	4	M. C.	10	0	3+	Asthma due to feathers and other inhalants; tolerates egg
	5	A. H.	14	0	+	No allergy
	6	J. R.	14	0	+	No allergy
	7	R. W.	12	0	+	No allergy
	8	J. W.	11	0	+	No allergy
	9	D. A.	10	0	+	Asthma due to feathers; tolerates egg
	10	J. R.	9	0	+	No allergy
Negative dermal reactors						
182				0	0	Negative reactors; no egg intolerance
130				0	Not tested	Negative reactors; no egg intolerance
Total						
322						Only 1 patient (0.3%) clinically sensitive to egg white Only 2 patients (1%) clinically sensitive to feathers

ANALYSIS OF DATA OBTAINED IN SURVEY OF EGG SENSITIVITY IN A SO-CALLED NONALLERGIC GROUP OF 322 CHILDREN

During the course of an investigation of the immunologic properties of influenzal and mumps virus vaccines, we studied a total of 322 children, consecutively admitted to the pediatric division of Sea View Hospital for tuberculosis, with reference to possible egg sensitivity. Our data are presented in Table 1. Included also are the results of tests with chicken feathers in 192 of these children.

Our survey revealed one clinically egg-sensitive child. This incidence, approximately 0.3%, closely agrees with an estimated 0.5% predicted in a previous paper.[9] It also tallies with the incidence in the literature described.

5. Pearson, R. S. B.: Observation on Skin Sensitivity in Asthmatic and Control Subjects, Quart. J. Med. **6**:165, 1937.

6. Carr, W. L., and Ratner, B.: The Results of Follow-Up Work with Infants in a Maternity Hospital, Am. J. Obst. & Gynec. **7**:73, 1924.

7. Smyth, F. S., and Bain, K. M.: Direct Skin Test in Allergy, J. Allergy **2**:316, 1931.

8. Balyeat, R. M.: Hereditary Factor in Allergic Disease, Am. J. M. Sc. **176**:332, 1928.

9. Ratner, B., and Untracht, S.: Allergy to Virus and Rickettsial Vaccines: I. Allergy to Influenza A and B Vaccine in Children, J. A. M. A. **132**:899 (Dec. 14) 1946.

INCIDENCE OF EGG SENSITIVITY IN ALLERGIC CHILDREN

In Table 2 are noted the dermal reactions to egg in children with eczema, ranging from 17.4 to 81.6%, reported in the literature.

TABLE 2.—*Egg Sensitivity Among Children with Eczema*

Source	No. Tested	Test Method*	Dermal Reactions to Egg White: Positive	Suggestive	Doubtful	Positive, %	Subjects
O'Keefe, E. S.: J. A. M. A. **78**:483 (Feb. 18) 1922	55	S	17	..	3	36.3	Children under 4 yr.
Sidlick, D. M., and Knowles, A. C.: Am. J. Dis. Child. **23**:316 (April) 1922	23	I	4	..	..	17.4	Children
Herman, H.: Am. J. Dis. Child. **24**:221 (Sept.) 1922	13	S	3	2	3	61.5	Children
Smyth, F. S., Bain, K., and Stallings, L.: J. A. M. A. **97**:1291 (Nov. 18) 1931	160	..	68	..	..	42.5	Infants
Corper, F. J.: Am. J. Dis. Child. **29**:355 (March) 1925	100	S	21	..	..	21.0	Infants under 1 yr.
Woringer, P.: Das Säuglingsekzem, Stuttgart, Wissenschaftliche Verlagsgesellschaft m. b. H., 1943	..	I	..	..	..	50.0	Infants
Moro [4]	49	..	40	..	..	81.6	Children, 41 under 3 yr.

* S indicates scratch test, I, intracutaneous test.

TABLE 3.—*Egg Sensitivity Among Children with Asthma*

Source	No. Tested	Positive Dermal Reactions to Egg Proteins: No.	%
Talbot, F. B.: New York J. Med. **17**:419, 1917	36	26	72.2
Herman, H.: Am. J. Dis. Child. **24**:221 (Sept.) 1922	16	3	18.8
Bullen, S. S.: New York J. Med. **29**:545, 1929	235	32	13.6
Peshkin, M. M.: Am. J. Dis. Child. **31**:763 (June) 1926	100	9	9.0
Rackemann, F. M.: J. Allergy **2**:113, 1931	207	24	11.6
Hill, L. W.: New England J. Med. **238**:657, 1948	100	21	21.0

TABLE 4.—*Positive Dermal Reactions to Egg White in Children with Eczema or Asthma According to Age*

Age Groups	Eczema: No. Tested	Eczema: Positive Reactions: No.	Eczema: Positive Reactions: %	Asthma: No. Tested	Asthma: Positive Reactions: No.	Asthma: Positive Reactions: %
Up to 2 yr	33	25	75.7	4	4	100
2 to 8 yr	56	22	39.3	84	19	22
8 to 18 yr	22	4	18.2	55	6	10.9
Total	111	51	45.9	143	29	20.3

Among children with asthma, as described in the literature, the dermal reactions to egg range between 9 and 72% (Table 3).

The influence of age and type of allergic manifestation on the incidence of egg sensitivity was subjected to further analysis (Table 4).

Considering the data from the standpoint of age grouping, it is seen, in the group with eczema, that 25, or 75.7%, of the 33 infants in the group up to 2 years

of age reacted to egg. In the 2- to 8-year old group the frequency of egg sensitivity drops to 39.3%. Above 8 years of age a further drop to 18.2% is noted.

Considering the data from the aspect of allergic manifestation, it is found that of 111 eczema patients, 51 reacted to egg white by scratch test. In other words, half (45.9%) of the eczematous children were egg sensitive. Among 143 asthmatic children, 20.3% reacted to egg white. Correlating the two factors, age grouping and allergic manifestation, it is interesting to note that the larger number of eczema cases fall into the younger age group, whereas there is a reversal in the situation in the cases of asthma, with a larger number of cases occurring in the older age groups. Hence, it is not surprising that we note a decreased incidence of egg sensitivity in patients suffering from asthma. A waning sensitivity to foods with increased age was suggested by Stuart and Farnham.[10]

In a previous study [9] we reported that 10.2% of a group of 108 allergic children presented positive reactions to egg white. However, only 4.6% were judged sensi-

TABLE 5.—*Egg White Sensitivity in 500 Children and a Clinical Evaluation of Sixty-Two of the Positive Reactors to Egg White*

Patients	Remarks
Total 500	102 (20.4%) showed positive reactions to egg white
62 of the 102 clinically evaluated	17 (27.4%)* were clinically sensitive to egg; 5 were exquisitely sensitive, 6 highly sensitive, and 6 moderately sensitive
	18 (29%) were clinically immune but showed a residual skin sensitivity
	27 (43.6%) had a residual dermal sensitivity but no history of egg intolerance

* This percentage, representing the number of children clinically sensitive to egg, is used to arrive at a final estimate of clinical egg sensitivity among allergic children (20.4% × 27.4% = 5.6%).

tive enough to warrant caution in the event that prophylactic injections of chick-embryo-cultured vaccine were to be given.

In order to check this estimate more accurately, 402 additional allergic children (consecutive patients) were given scratch tests which gave a total of 500 patients (Table 5). We found that 102 patients, 20.4%, reacted positively to egg protein.

To correlate dermal and clinical sensitivity, 62 of the 102 patients were further evaluated for reactions from egg ingestion. Seventeen (27.4%) had clinical manifestations. From this it would appear that only about one-quarter of skin-sensitive patients present correlative clinical manifestations. Therefore, on the basis of our experience with 500 cases we may infer that about 5% of all allergic children are clinically responsive to egg. This compares favorably with the estimation of 4.6% made previously.[9]

VALIDITY OF EGG ALLERGY AS DETERMINED BY DERMAL TEST

In the eczematous infant a dermal reaction to egg is encountered so frequently that its clinical significance is often questioned. It is especially enigmatic because the diet of many of these infants consists solely of milk.

10. Stuart, H. C., and Farnham, M.: Acquisition and Loss of Hypersensitiveness in Early Life, Am. J. Dis. Child. **32**:341 (Sept.) 1926.

The demonstration of intrauterine sensitization by Ratner and associates and others [11] has presented evidence for the passage of substances via the placenta, including foreign sera, food proteins, antitoxins, bacteria, and the Rh factor, among others.[12] Likewise, the concept of the passage of proteins through the intestinal wall has been established.[13] The demonstration of the passage of antigens through such living membranes gives us a clue to the manner in which spontaneous food allergies may arise.

One of the difficulties in substantiating intrauterine sensitization in the newborn is the lack of reactivity of the skin at this age. It has been demonstrated by Ruh and McClelland,[14] Kuttner and Ratner,[15] and others that a temporary skin inertia is present in the newborn period. Nevertheless, occasional instances of skin reactivity in the newborn have been reported. Balyeat [8] found a positive reaction to egg in a 3-day-old infant, and Lyon [16] was able to elicit reactions to corn and bean in a newborn infant.

Schloss and Worthen,[17] Blackfan,[1] Smyth and Bain,[7] Ratner,[11b] and others reported cases in which positive reactions to egg white were obtained in infants

TABLE 6.—*Dermal Egg White Reactors Among Allergic Children Whose Mothers Gave a Positive History of Excessive Ingestion of Egg During Pregnancy*

Total number of allergic children investigated	248
Number and percentage of the above 248 children who showed sensitivity to a variety of foods* related to excessive ingestion by the mother during pregnancy	75 (30%)
Number and percentage of the above 75 children who reacted to egg white	42 (56%)
Number and percentage of the above 42 egg-white-sensitive children who gave a history of allergic reaction to egg white on first ingestion of this food	21 (50%)

* In the order of frequency, sensitivities to other foods after egg, were vegetables 13.6%, milk 9.3%, fish 8%, wheat 6.7%, nut 5.2%. Spices, orange, condiments, chocolate, and meats were below 5%.

who had never eaten eggs. In work done a number of years ago on the influence of the antepartum diet in the production of intrauterine sensitization, we found

11. (*a*) Ratner, B.; Jackson, H. C., and Gruehl, H. L.: Transmission of Protein Hypersensitiveness from Mother to Offspring: V. Active Sensitization in Utero, J. Immunol. **14**:303, 1927. (*b*) Ratner, B.: Possible Causal Factor of Food Allergy in Certain Infants, Am. J. Dis. Child. **36**:277 (Aug.) 1928. (*c*) Needham, J.: Chemical Embryology, London, Cambridge University Press, 1931.

12. Levine, P., and Katzin, E. M.: Isoimmunization in Pregnancy and Varieties of Isoagglutinins Observed, Proc. Soc. Exper. Biol. & Med. **45**:343, 1940. Wiener, A. S., and Peters, H. R.: Hemolytic Reactions Following Transfusions of Blood of Homologous Group, with 3 Cases in Which Same Agglutinogen Was Responsible, Ann. Int. Med. **13**:2306, 1940.

13. Ratner, Jackson, and Gruehl.[11a] Schloss, O. M.: Intestinal Absorption of Antigenic Protein, in Harvey Lectures, 1924-25, Philadelphia, J. B. Lippincott Company, 1925, p. 156. Walzer, M.: Studies in Absorption of Undigested Proteins in Human Beings, J. Immunol. **14**:143, 1927. Ratner, B., and Gruehl, H. L.: Passage of Native Proteins Through the Normal Gastro-Intestinal Wall, J. Clin. Invest. **13**:517, 1934.

14. Ruh, H. O., and McClelland, J. E.: Comparison of Diphtheria Immunity in the Mother and in the New-Born, Am. J. Dis. Child. **25**:59 (Jan.) 1923.

15. Kuttner, A. G., and Ratner, B.: Importance of Colostrum to the New-Born Infant, Am. J. Dis. Child. **25**:413 (June) 1923.

16. Lyon, G. M.: Allergy in an Infant of Three Weeks, Am. J. Dis. Child. **36**:1012 (Nov.) 1928.

17. Schloss, O. M., and Worthen, T. W.: The Permeability of the Gastroenteric Tract of Infants to Undigested Protein, Am. J. Dis. Child. **11**:342 (May) 1916.

that of 248 cases of allergy in children (Table 6), 75, or 30%, gave a history of excessive ingestion of one or more foods by the pregnant mother. The largest number of patients, 56%, reacted to egg white, and a history of excessive egg indulgence was obtained. An allergic reaction to the first contact with egg was obtained in 50% of these cases. Schloss [18] had a similar experience, for he observed that in 16 of 33 cases symptoms developed the first time a specific food was eaten.

Because of the frequency of egg white sensitivity, some investigators ascribed the actual clinical disease to unknown "x" factors [19] and endeavored to explain such frequency on the basis of a heterophile mechanism, or cross reaction to chicken feathers. We have subjected this thesis to analysis in Table 1 and found that feather sensitivity was of high order in Case 4, of a 10-year-old in whom no egg white sensitivity was found; in Case 1 a high order of egg white sensitivity was present with a negligible feather sensitivity. In six other cases feather sensitivity of moderate degree was present, with no evidence of egg white sensitivity.

Cross reactivity to egg through early feather sensitivity would be difficult to understand, for egg white outstrips feather sensitivity in the early period, and feathers become an important factor chiefly in older children.

A so-called natural heterophile may prove to be a specific antibody produced by an ingested food. A striking instance was reported by Friedberger and Jarre.[20] In their experiment antidog serum was obtained by injecting serum of a dog into a rabbit. The serum precipitated dog serum in up to 1:20,000 dilution, but it also precipitated the sera of horse and donkey in the same dilution. It was later discovered that the dog from which the serum was obtained had been fed horse meat for many years. In this instance, therefore, were it not for the evidence of the horse meat in the dog's diet, the presence of the horse serum antibody would have been explained on the heterophile basis. French investigators [21] have reported that human subjects who consumed horse meat went into anaphylactic shock after receiving a first injection of equine antiserum.

It seems reasonable to draw the conclusion from this evidence that specific sensitivity to egg white, rather than a cross reaction to feathers or natural heterophile, explains the preponderance of egg-white reactivity in infants.

It is interesting to note that egg white produces reactions other than those related to allergy. For example, it has been shown [22] that the rat may be primarily sensitive, since this animal will demonstrate anaphylactoid reactions to egg white on initial injection. It has also been shown [23] that guinea pigs will react with

18. Schloss, O. M.: Allergy in Infants and Children, Am. J. Dis. Child. **19**:433 (June) 1920

19. Sulzberger, M. B.: Dermatologic Allergy, Springfield, Ill., Charles C Thomas, Publisher, 1940.

20. Friedberger, E., and Jarre, H.: Ueber aspezifische präzipitierende Sera, Ztschr. Immunitätsforsch. **30**:351, 1920.

21. Bernard, L., and Paraf, J.: Accidents de la sérothérapie antituberculeuse par le sérum de Vallée, Bull. Soc. d'études scient. sur la tuberc. **1**:64, 1911. Bernard, L.; Debré, R., and Porak, R.: Sur la présence dans le sang circulant de l'albumine hétérogène après l'ingestion de viande crue, J. physiol. et path. gén. **14**:971, 1912. Billard, G.: Hippophagia et anaphylaxie au sérum de cheval, Compt. rend. Soc. biol. **73**:462, 1912.

22. Leger, J.; Masson, G., and Prado, J.: Hypersensitivity to Egg White in the Rat, Proc. Soc. Exper. Biol. & Med. **64**:366, 1947.

23. Cohen, S. J.: Protein Fever: The Effect of Egg White Injection on the Dog, J. Lab. & Clin. Med. **5**:285, 1920.

apparent nonspecific fever, while dogs sustain the injection of egg white with little effect. Egg-white injury,[24] perhaps related to biotin lack, has also been described. Egg yolk when mixed with snake venom possesses peculiar toxic powers.[25]

These phenomena, which apparently bear no relation to the antigen-antibody reaction, are evidence of other physiological disturbances which may be caused by egg but do not militate against the body of evidence for real egg sensitivity in the explanation of major and minor allergic syndromes.

COMMENT

The diagnosis of clinical egg sensitivity cannot be made on the basis of the skin test alone. Positive skin reactions to egg outnumber their clinical significance, and a positive skin reaction with egg may connote either a marked clinical intolerance or a limited tolerance for egg, or, on the other hand, it may indicate a residual skin reactivity in a person who has long overcome his clinical intolerance. Such cases have been described in a previous paper[9] in which we endeavored to assay the importance of egg allergy in relation to the administration of viral and rickettsial vaccines:

> Cases 6 (B. H.) and 11 (B. W.) are those of 2 children who ten years prior to this study were known to be extremely sensitive [clinically] to egg white. Over a period of years both children were given egg white in gradually increasing doses, and both have tolerated egg in regular amounts in their diets for about eight years. Skin tests with egg white show that the two have only a residual dermal sensitivity to egg by the scratch test and only a moderately positive response by the intradermal route. The [viral] vaccine reaction was only moderate in degree.

Since we had the opportunity to follow these and other cases over a long period of years and found that these children, who were extremely sensitive to egg both clinically and dermally when they were first observed, gradually lost the clinical sensitivity, but preserved a mild skin sensitivity, we felt justified in describing the mild reactivity as "residual dermal sensitivity" which has little or no clinical significance. This undoubtedly applies to the interpretation of skin tests with other foods as well.

In previous writings we have voiced the opinion that were it not for the defense mechanisms which man and animal have developed throughout the ages, they would have succumbed to the ingestion of new and strange protein foods. The absorption of protein occurs under normal conditions with greater regularity than is generally held. This normal absorption may conceivably serve the useful purpose of constantly maintaining the body in a state of immunization against habitual protein diets. A spontaneously acquired immunity to egg protein is readily conceivable because of the common use of egg in the diet, not only as a food per se but more especially in the preparation of a variety of foods.

The evaluation of a sensitivity to egg white must therefore take into consideration: (1) the history of egg sensitivity as noted by the patient; (2) the evidence for sensitivity by clinical test, and, finally, (3) a careful interpretation of the skin test, i. e., (*a*) if the reaction remains local and limited in area, the sensitivity is

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24. King, R. R., Jr.: Advancement in Biotin Research, J. Bowman Gray School Med. **2**:75, 1944.

25. Boquet, P.; Dworetzky, M., and Essex, H. E.: Physiologic Responses of Certain Animals and Isolated Preparations to Mixtures of Snake Venom and Egg Yolk, Am. J. Physiol. **161**:561, 1950.

usually of a low order; (*b*) if the local reaction is extensive and is coupled with a systemic reaction, e. g., urticaria and dyspnea, then the sensitivity is of a high order.

In extremely rare instances a negative or low order of dermal reaction may be accompanied with a systemic reaction.[26]

The evaluation of these criteria in relation to the use of chick-embryo-propagated viral and rickettsial vaccines is the subject of forthcoming studies.

SUMMARY AND CONCLUSIONS

Our previous estimates that only 0.5% of the general population and only 5% of allergic persons who are sufficiently sensitive to egg to warrant special precautions in the administration of chick-embryo-propagated viral and rickettsial vaccines are further corroborated.

In a group of 322 so-called nonallergic children, egg sensitivity, as judged by the presence of clinical sensitivity and a positive skin reaction, was found in 0.3%.

In a group of 500 known allergic children, 20.4% were found to be skin sensitive to egg white. However, only 5.6% of the entire group were found clinically sensitive to egg white as well. The remainder of the 20.4% had a residual skin sensitivity without clinical significance.

An inordinately high incidence of egg reactivity is found in young allergic infants. Hence, egg sensitivity is more frequently associated with eczema than with asthma. The incidence of egg-white sensitivity wanes with age.

The frequency of egg reactions in early infancy we attribute to intrauterine sensitization.

Dermal reactivity to egg protein meets the criteria set for the allergic phenomenon of antigenicity, specificity, and dependence upon antigen-antibody reaction, and therefore follows the pattern of reaction which is evident for all foreign proteins which have by devious and, at times, not very obvious routes found their way into the body.

The diagnosis of egg sensitivity cannot be made on the basis of the skin test alone, for positive skin reactions to egg outnumber their clinical significance. A positive skin reaction to egg may connote (*a*) a residual skin reaction in a person who has long overcome his clinical intolerance, (*b*) a limited tolerance for egg, or (*c*) a marked clinical intolerance for egg. A negative reaction may on occasion be encountered in a person with a marked clinical sensitivity. Hence, the skin reaction must be considered in relation to the complete clinical picture.

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26. Ratner, B.: Treatment of Milk Allergy and Its Basic Principles, J. A. M. A. **105**:934 (Sept. 21) 1935.

CONGENITAL HEART DISEASE FOLLOWING MATERNAL RUBELLA DURING PREGNANCY

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IN THE year 1941 Gregg [1] called attention to the frequent occurrence of congenital cataracts in infants born of mothers who had had German measles in the early months of pregnancy. Many other investigations confirmed these observations, and within a short time it became clear that such infants frequently suffered not only from congenital cataracts but also from deafness, congenital heart disease, and mental retardation.

Wesselhoeft [2] collected a series of 521 cases from the Australian, American, and British literature of infants born following maternal rubella during pregnancy, In this group he found that 221 had eye defects, 243 had impaired hearing, and 221 had signs indicating the presence of congenital heart disease.

In spite of the fact that so large a proportion of these children have cardiac defects, we have been unable to find in the literature any study devoted specifically to a consideration of the various anatomic lesions encountered.

It has therefore seemed worth while to record our findings in a small group of patients who have come under our observation. Our material consists of 1,366 private patients with congenital heart disease seen by one of us (S. G.) in the past few years. Cyanosis was present in 645. Every mother was questioned concerning any illness during her pregnancy and particularly as to German measles. A history of German measles was obtained in 17 instances. The table summarizes the findings in these 17 cases.

It is seen that a diagnosis of patent ductus arteriosus was made in 14 cases. In 10 of these the diagnosis was confirmed at operation. It is of interest that in four of these 10 cases an additional congenital cardiac malformation was present. T. M. was found at operation to have a marked thrill in the region of the pulmonary valve after the ductus had been clamped, suggesting the presence of pulmonary stenosis. On this account, the ductus was left intact. S. C. was found preoperatively to have rather faint femoral pulsations with a barely audible femoral thud. The blood pressure in the arms was 130/20; that in the legs was

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1. Gregg, N. M.: Congenital Cataract Following German Measles in the Mother, Tr. Ophth. Soc. Australia **3**:35, 1941.

2. Wesselhoeft, C.: Medical Progress: Rubella (German Measles), New England J. Med. **236**:978 (June 26) 1947.

98/75. Coarctation of the aorta was suspected, and it was confirmed at operation. The ductus was severed at its point of junction with the pulmonary artery, and the ductus and coarctation were removed en masse.

T. D. was found postoperatively to have a blowing Grade 3 to 4 systolic murmur at the base of the heart. A thrill was palpable. J. L. had postoperatively practically the same findings as T. D. A systolic murmur accompanied with a thrill was present in the third left interspace. We believed that a septal defect was present in each of these patients. The murmur could not have been due to incomplete obliteration or recanalization of the ductus, as the ductus was severed in both instances.

Data for Seventeen Cases of Congenital Heart Disease Following Maternal Rubella During Pregnancy

Patient	Age, Yr.	Maternal Rubella, Mo. of Pregnancy	Cardiac Lesion	Accompanying Lesions	Closure of Ductus
J. A.	6	1st-2d	Patent ductus	Cataracts; deafness	+
C. B.	3	3d	Patent ductus	None	..
E. A.	9	3d-4th	Patent ductus	None	..
M. K.	5	2d	Patent ductus	None	+
D. K.	4	2d	Patent ductus	Deafness	+
J. M.	12	2d	Patent ductus	Bilateral cataracts	+
K. M.	3	2d-3d	Patent ductus	Deafness	..
W. W.	4	2d	Patent ductus	Cataract, right eye; coloboma	+
S. O.	11/12	1st	Patent ductus	None	..
C. G.	4	2d	Patent ductus	Cataract, left eye; strabismus	+
T. M.	4	2d	Patent ductus; pulmonary stenosis	Cataract, right eye; strabismus	Ductus exposed, not obliterated
S. C.	4	2d-3d	Patent ductus; coarctation of aorta	Cataract, right eye	+
T. D.	6	3d-4th	Patent ductus; septal defect	None	+
J. L.	7	2d-3d	Patent ductus; septal defect	None	+
J. C.	7	1st	Defect of auricular septum	None	..
D. R.	19/24	5th	Defect of ventricular septum	None	..
J. B.	10/12+	2d	Tetralogy of Fallot	Cataract, left eye	..

There were three patients in whom there were no symptoms or signs suggesting a patent ductus arteriosus. J. C. on physical examination revealed marked cardiac enlargement. The apex thrust was in the fifth left interspace in the anterior axillary line. A Grade 3 systolic murmur was maximal in the third left interspace. A diastolic murmur was heard at the base of the heart, and over a limited area at the apex a presystolic murmur was heard. The fluoroscopic examination showed marked enlargement of the right atrium and ventricle. There was a very prominent pulmonary artery segment together with a hilar dance. We considered the findings suggestive of a defect of the auricular septum, possibly complicated by mitral stenosis.

D. R. was a well-developed, well-nourished infant weighing 24 lb. (10,900 gm.) at the age of 19 months. He did not present the usual slender body build of the German measles baby. Examination of the heart revealed a harsh rasping Grade 5

systolic murmur over the precordium, maximal in the fourth left interspace. A coarse thrill was palpable. The findings seemed typical of a defect of the ventricular septum. There was no other stigma of maternal rubella. It will be noted that in this case the German measles occurred in the fifth month of pregnancy. Inasmuch as the heart is completely formed at a much earlier period in fetal life, the heart lesion was probably in no way associated with the mother's illness.

J. B. was the one cyanotic infant in the entire group. He had been cyanotic from birth. His red blood cell count was 8,230,000, the hemoglobin level 16 gm. The physical signs, roentgenographic, fluoroscopic, and electrocardiographic findings were typical of a tetralogy of Fallot. A cataract was present in the left eye.

COMMENT

Although one cannot draw definite conclusions from this small group of cases, there are certain features which seem worthy of emphasis. The high proportion of instances of patent ductus arteriosus is impressive. It is also of interest that of the 10 patients studied at operation, a complicating lesion was encountered in four. For purposes of comparison, we reviewed 140 cases of patent ductus arteriosus in otherwise healthy children who have been operated on during the past few years. We found only six cases in which a significant murmur persisted after the ductus had been severed, an incidence of 4.3%. Gross and Longino,[3] in reporting 412 surgically treated patients, found signs suggesting an additional congenital cardiac defect in 24 patients, an incidence of 5.8%. The finding of an additional lesion in four of 10 cases of proved patent ductus arteriosus following maternal rubella at least suggests that complicating lesions are much more frequent in these patients than in otherwise normal children.

SUMMARY

In 1,633 cases of congenital heart disease a history of maternal rubella was obtained in 17 instances, approximately 1%.

Of these 17 patients, 14 were believed to have a patent ductus arteriosus, and the diagnosis was confirmed by operation in 10.

Of the 10 patients studied at operation, an additional cardiac defect was encountered in four.

Only one of the 17 patients fell into the cyanotic group.

3. Gross, R. E., and Longino, L. A.: The Patent Ductus Arteriosus: Observations from 412 Surgically Treated Cases, Circulation **3**:125 (Jan.) 1951.

Q-T_c INTERVAL IN DIAGNOSIS OF RHEUMATIC FEVER

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IN THE year 1947 Taran and Szilagyi[1] proposed a prolonged electrical systole (the Q-T interval of the electrocardiogram) as a sensitive and reliable diagnostic aid in detecting the presence and severity of active rheumatic carditis. These observations were subsequently confirmed by Abrahams.[2] However, several recent independent studies [3] indicate that the Q-T interval may not be consistently prolonged in acute rheumatic carditis. We have recently reviewed the problems of diagnosis in rheumatic fever and have cited the need for more perceptive diagnostic tools.[4] The present study of the Q-T interval attempts to evaluate the usefulness of this controversial measurement in a well-defined body of rheumatic and control material.

MATERIAL AND METHODS

The clinical material employed in the present study has been described at length elsewhere.[4] Clinical, laboratory, roentgenologic, and electrocardiographic findings have been reviewed in detail. The table indicates the distribution of cases in arbitrary descriptive groups. For present purposes, cases in groups I, IIa, and IIb have been combined as cases of active rheumatic fever, and groups IVa, IVb, Vb, Vc, VI, and IX are not included. The Q-T interval was not considered in the diagnosis or grouping of the material. Electrocardiograms were made with a direct writing machine. Each tracing consisted of three standard limb leads, three augmented unipolar limb leads, and six unipolar chest leads (V_1, V_2, V_3, V_4, V_5, and V_6). The Q-T interval and the corresponding cycle length were measured with the aid of a hand magnifying lens in the shortest

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From the Departments of Pediatrics and Medicine, University of Rochester School of Medicine and Dentistry, and the Strong Memorial-Rochester Municipal Hospitals.

1. Taran, L. M., and Szilagyi, N.: The Duration of Electrical Systole (Q-T) in Acute Rheumatic Carditis in Children, Am. Heart J. **33**:14, 1947.

2. Abrahams, D. G.: The Q-T Interval in Acute Rheumatic Carditis, Brit. Heart J. **11**:342, 1949.

3. Pokress, M. J., and Goldberger, E.: A Study of the Q-T Interval in Rheumatic Fever, Am. Heart J. **38**:423, 1949. Epstein, N., and Gardam, J. D.: A Study of the Q-T_c Interval in the Electrocardiogram in Rheumatic Fever, J. Pediat. **36**:583, 1950. Craige, E.; Alimurung, M. M.; Bland, E. F., and Massell, B. F.: The Q-T Interval in Rheumatic Fever, Circulation **1**:1338, 1950.

4. Joos, H. A., and Katsampes, C. P.: A Community Study of Rheumatic Fever, Am. J. Dis. Child. **82**:37 (Jan.) 1952.

and the longest cycle in each of three limb leads and three chest leads, including at least two left precordial leads. The average of these intervals was then obtained, and the Q-T interval was corrected for heart rate, using the modified Bazett's formula [5]:

$$Q\text{-}T_c = \frac{\text{Q-T (in seconds)}}{\sqrt{\text{cycle length (in seconds)}}}$$

A series of tracings was obtained on most patients, particularly in the rheumatic groups. The first tracing or the first representative tracing from each patient was used in the analysis of the data.

In a previous study [6] we found a mean Q-T_c value of 0.405 second in 100 normal infants and children. The standard deviation was ±0.010, and the measurement ranged from 0.365 to 0.424 second. There were no significant age or sex differences.

RESULTS

The Q-T_c interval was significantly prolonged, i.e., greater than 0.424 second in 84% of cases of active rheumatic fever (Charts 1 and 4). In 12% of the active cases the Q-T_c interval was in the doubtful range, 0.415 to 0.424. Only 4% of cases with clinical and laboratory evidence of rheumatic activity had Q-T_c values of

Descriptive Classification of Clinical Groups *

Group	Description	No. of Cases
I	Acute rheumatic fever, first attack	36
IIa	Protracted rheumatic fever, acute reactivation	9
IIb	Protracted rheumatic fever, subacute	7
III	Quiescent rheumatic fever	18
IVa	Chorea, no supporting evidence of rheumatic fever	2
IVb	Same as IVa, but chorea doubtful	6
Va	Suspected rheumatic fever, acute or protracted	35
Vb	Rheumatic fever, doubtful activity	5
Vc	Quiescent rheumatic fever, diagnosis of original rheumatic fever uncertain	29
VI	Congenital heart disease, no rheumatic fever	14
VII	Acute infectious diseases	70
VIII	Miscellaneous diseases	35
IX	Normal children	81

* Classification taken from previous study (Am. J. Dis. Child. **83**: 37 [Jan.] 1952).

less than 0.415. Acute rheumatic pericarditis was diagnosed in two cases in which Q-T_c intervals were in the lower range (Chart 1). In both cases the Q-T intervals lengthened considerably as pericarditis subsided. No patient with active rheumatic fever had a Q-T_c interval shorter than 0.407 second (normal mean, 0.405).

Among rheumatic children whose disease was quiescent, Q-T_c intervals were significantly prolonged (greater than 0.424) in 12%, doubtful (0.415 to 0.424) in 19%, and normal (less than 0.415) in 69% (Charts 1 and 4). True quiescence of the disease is notably difficult to establish by any means. It has been suggested [7] that a prolonged Q-T_c interval in cases in which the disease is clinically inactive may indicate continuing low-grade rheumatic activity. Without more prolonged observations, our study is not informative in this regard.

Charts 2 and 4 show the range, scatter, and distribution of the Q-T_c interval in cases of suspected active rheumatic fever in which the diagnosis could neither be

5. Bazett, H. C.: An Analysis of the Time-Relations of Electrocardiograms, Heart **7**:353, 1918-1920. Taran and Szilagyi.[1]

6. Yu, P. N. G.; Joos, H. A., and Katsampes, C. P.: Unipolar Electrocardiogram in Normal Infants and Children, Am. Heart. J. **41**:91, 1951.

7. Taran and Szilagyi.[1] Abrahams.[2]

confirmed nor excluded. In 32 such cases, the Q-T_c interval was prolonged in 56%, doubtful in 9%, and normal in 35%. Again, only a prolonged series of clinical and electrocardiographic observations will differentiate the true rheumatics and demonstrate the diagnostic value of the Q-T_c interval in such cases. However, the consistent prolongation of the Q-T_c interval in cases of known active disease suggests that active carditis may be likelier in cases in which the disease is clinically quiescent and in cases of suspected active rheumatic fever if the Q-T_c interval is significantly lengthened.

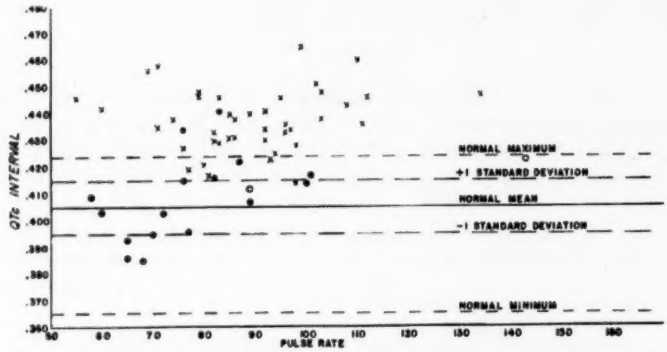

Chart 1.—Distribution of the Q-T_c interval in active and quiescent rheumatic fever. Cases of active rheumatic fever (43) are indicated by crosses; cases of active rheumatic fever with pericarditis (2), by hollow circles; cases of quiescent rheumatic fever (16), by solid circles.

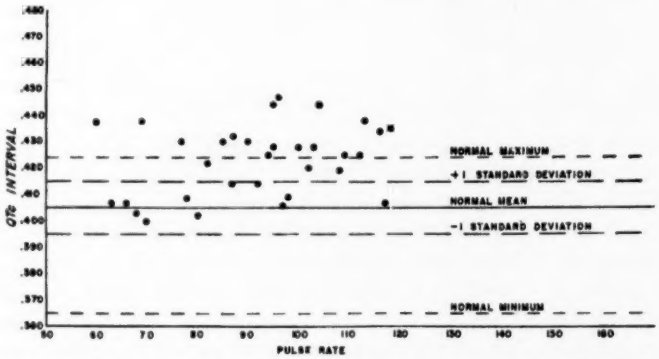

Chart 2.—Distribution of the Q-T_c interval in the cases of suspected rheumatic fever. Cases (32) are indicated by solid circles.

Groups of infectious and miscellaneous diseases were studied in order to determine to what extent nonrheumatic illness may influence the Q-T_c interval. The results are shown in Charts 3 and 4. Ten per cent of patients with acute infectious diseases and 16% of patients with miscellaneous diseases showed prolongation of the Q-T_c interval. The measurement was doubtful in 15% of each group and normal in 75% of the former and 69% of the latter patients. Occasional prolongation

of the Q-T_e interval in these nonrheumatic patients deserves additional attention. The diagnoses of these cases are indicated in Chart 3. Most of the cases of acute infectious disease with a prolonged Q-T_e interval were cases of acute poliomyelitis and have been discussed elsewhere.[8] The other two cases are briefly presented:

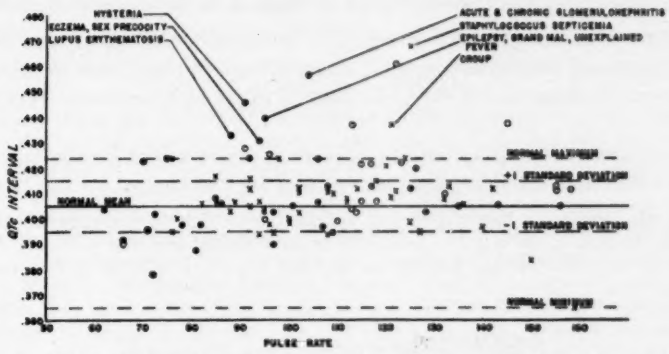

Chart 3.—Distribution of the Q-T_e interval in control groups. Cases of acute infectious disease (66) are indicated by crosses; cases of acute infectious disease, acute poliomyelitis (21), by hollow circles; cases of miscellaneous diseases (32), by solid circles.

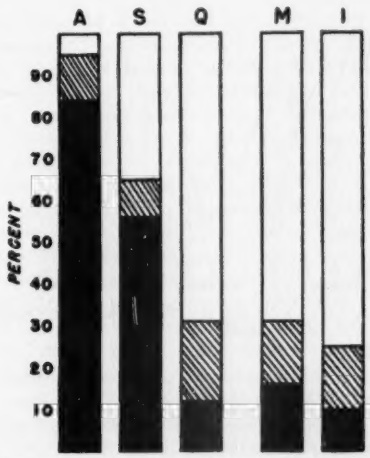

Chart 4.—Percentage distribution of the Q-T_e interval in rheumatic and control groups. *A* indicates data for cases of active rheumatic fever; *S*, suspected rheumatic fever; *Q*, quiescent rheumatic fever; *M*, miscellaneous diseases; *I*, acute infectious diseases. Black areas indicate percentage of cases with Q-T_e intervals exceeding 0.424 second; lined areas indicate percentage of cases with Q-T_e intervals between 0.415 and 0.424 second; white areas indicate percentage of cases with Q-T_e intervals less than 0.415 second.

The patient with croup recovered rapidly and uneventfully. Pathogenic bacteria were not isolated, and during the three-day hospitalization no supporting clinical evidence of cardiovascular disease was obtained. The electrocardiogram was normal except for the Q-T_e interval.

8. Joos, H. A., and Yu, P. N. G.: Electrocardiographic Observations in Poliomyelitis, Am. J. Dis. Child. **80**:22 (July) 1950.

The patient with hemolytic Staphylococcus aureus septicemia and sinusitis at first was suspected of having rheumatic fever. A labile heart rate, changing heart sounds, and tic-tock rhythm suggested possible acute carditis. Therapeutic doses of sodium salicylate were given for seven days until the diagnosis became clear, after which the Q-T_c value rose from 0.468 to 0.483 and then fell to 0.435 two weeks later as the infection was treated successfully with penicillin and aureomycin. Diphasic T waves appeared in lead I, with an inverted T wave in lead aV_L during the acute course. The T waves returned to normal as the Q-T_c interval shortened.

Myocarditis is known to occur during acute infections of all types,[9] and the associated clinical and electrocardiographic changes may simulate those in acute rheumatic fever. Prolongation of the Q-T_c interval might be expected to occur in such cases.

Prolongation of the Q-T_c interval in cases of noninfectious disease occurred in five patients (Chart 3). Four of these five cases are summarized briefly:

Slight left ventricular hypertrophy was suspected from the electrocardiogram and from fluoroscopic findings in the case of eczema with probable sexual precocity (patient J. C.). The P-R interval was of borderline duration for age and heart rate, and the Q-T_c interval was prolonged.

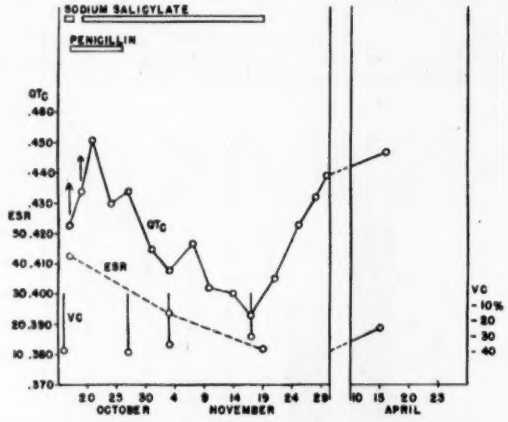

Chart 5.—Changes in the Q-T_c interval, the Wintrobe sedimentation rate (ESR), and vital capacity (VC) in the case of C. V. reported.

J. F., a child with grand mal epilepsy, had a consistent low-grade fever of about 38 C. and a prolonged Q-T_c interval during his hospital stay of three weeks. A specific infectious cause for the fever could not be established. Except for an antistreptolysin O titer of 625, there was no evidence of rheumatic or other cardiovascular disease.

A prolonged Q-T_c interval and ST-T wave abnormalities in the precordial leads were found in the case of G. V., hospitalized for an acute exacerbation of chronic glomerulonephritis. The Q-T_c interval shortened and the ST-T wave changes reverted to normal as the acute process subsided. There was no hypertension during this episode.

H. S. suffered an acute attack of disseminated lupus erythematosus. Myocardial disease was evident clinically, and the electrocardiogram showed consistent prolongation of the Q-T_c interval, many ST-T wave abnormalities in both limb and chest leads, and transient auriculoventricular conduction delay. This child had a persistent hypopotassemia, but the Q-T_c interval remained prolonged even when the serum potassium was maintained at normal levels.

9. Rantz, L. A.: Myocarditis in Infections, with a Selected Bibliography, Stanford M. Bull. **7**:12, 1949.

It is evident that prolongation of the Q-T_c interval in these cases was frequently associated with clinical and electrocardiographic evidence suggesting myocardial disease.

The progress of rheumatic disease was observed in detail in many patients during the year-long course of the study. The representative case of C. V. is summarized in Chart 5, in which changes of the Q-T_c interval may be compared with the erythrocyte sedimentation rate (Wintrobe) and the vital capacity (Wilson [10]).

REPORT OF A CASE

C. V., an 11-year-old white girl, was admitted to the Rochester Municipal Hospital on Oct. 15, 1949, with her second acute attack of rheumatic fever. She had been hospitalized for three months early in 1949 for her first rheumatic episode. Continuing low-grade rheumatic activity had been suspected. On the day preceding the present admission fever, cough, dyspnea, tachycardia, and anorexia developed. At the time of examination the child was pale, apprehensive, and somewhat short of breath. Her temperature was 39.5 C., her pulse rate 148. The heart was enlarged; the sounds were muffled, and there was a harsh, loud, high-pitched systolic murmur loudest at the apex and transmitted laterally. The white blood cell count was 16,600, with 93% neutrophiles. The hemoglobin (Sahli) was 17.4 gm. per 100 cc., the corrected Wintrobe sedimentation rate 46 mm. an hour, and the vital capacity —37%. The antistreptolysin O titer was 500 and the antihyaluronidase 1:80. Roentgen examination at the time of admission showed a moderately enlarged left ventricle and an increase in the interstitial pulmonary densities at the right base. The electrocardiogram showed delayed auriculoventricular conduction and a Q-T_c interval of greater than 0.432 second. The ends of the T waves were overlapped by succeeding P waves, so that the Q-T interval was measured only to its intersection with the P wave. Administration of therapeutic doses of sodium salicylate was begun at once but was discontinued after 24 hours in favor of penicillin administration because the pneumonia was thought to be bacterial. Salicylate therapy was begun again on Oct. 19 after the patient had failed to respond to penicillin. Administration of the latter drug was continued for nine days, although a diagnosis of rheumatic pneumonia was made. Therapeutic doses of sodium salicylate were continued for 34 days. Vitamin K was given in addition, and the child was kept at complete rest. Improvement was steady after the first week. Her temperature was normal within 48 hours after sodium salicylate therapy was resumed. The pneumonia cleared promptly, and the heart became somewhat smaller. The tachycardia, with a rate of more than 110 a minute, persisted for 20 days. The P-R interval remained prolonged, but the Q-T_c interval shortened to normal levels after 14 days of salicylate therapy. The sedimentation rate declined gradually, and the vital capacity improved slightly. After sodium salicylate was discontinued on Nov. 19, all clinical evidence of improvement was sustained, and the patient continued to feel well. However, the Q-T_c value rose consistently from 0.395 to 0.439 before her discharge on the 46th hospital day. Convalescent hospital care was refused, and she was sent home to remain at complete rest. Three months later she was admitted to the Rochester Convalescent Hospital for Children with active subacute rheumatic fever. The sedimentation rate was 19 mm. an hour, the hemoglobin 14.5 gm., the white blood cell count 21,000. The electrocardiogram showed a prolonged P-R interval and a Q-T_c interval of 0.447 second. The high and wide P waves suggested auricular hypertrophy and dilatation.

The declining Q-T_c interval during this patient's acute course correlated with her clinical improvement. When the Q-T_c value reached 0.393, the rheumatic process may have become completely quiescent. However, her subsequent course shows clearly that this was not true. We have been impressed by the effect of therapeutic blood levels of salicylate in shortening the Q-T_c interval This effect is separate from that of the drug on the rheumatic process itself. Taran and Ordorico [11] have

10. Wilson, M. G.: Rheumatic Fever, New York, Commonwealth Fund, 1941.

11. Taran, L. M., and Ordorico, D.: Electrical Systole in Acute Rheumatic Pericarditis, J. Pediat. **36**:466, 1950.

recorded a similar opinion. Therefore, the Q-T_c interval cannot be used as an accurate guide to rheumatic activity if the patient is receiving therapeutic doses of a salicylate. The case of V. C. suggests that the sharply rising Q-T_c interval after cessation of salicylate therapy might have foretold the continuing rheumatic difficulties.

COMMENT

The study of electrical systole (the Q-T interval) employs the electrocardiogram to evaluate a physiologic property of the myocardium rather than its anatomic continuity. Physiologic measurements are subject to many biologic influences, each of which must be understood in order to make the measurement of value in prediction. The Q-T interval is no exception. Pericarditis,[11] for example, may shorten the Q-T_c interval appreciably during acute rheumatic fever, perhaps even in cases in which a clinical diagnosis of pericarditis cannot be made. Digitalis may shorten the Q-T interval to normal or less, even with fulminating acute carditis and heart failure. Salicylate may also shorten the Q-T interval. Electrical systole may be prolonged to doubtful or abnormal levels by such influences as apprehension or excitement, exercise, hypocalcemia, hypopotassemia, quinidine, hypertension, and cardiac decompensation. In the presence of a cardiac arrhythmia other than a respiratory sinus arrhythmia, the Q-T interval may be variable and entirely unpredictable. The mechanisms whereby the Q-T interval is affected under such heterogeneous circumstances are not clearly understood. It is possible, therefore, that undiscovered metabolic influences may affect the Q-T interval. Certainly all known factors other than carditis which can affect the Q-T interval must be taken into account in evaluating the measurement in each case.

Similarly, the establishment of a reliable physiologic measurement requires standardization of technique so that the measurement is predictable under controlled circumstances. Taran and Szilagyi[12] have shown that the method of measurement of the Q-T_c interval is of great importance. They attributed the variation in results reported by other investigators to the discrepancy in methods employed. They recommend the following technique. All cycles in a 15-cm. strip of the electrocardiogram in each of the three limb leads and in each of three chest leads (positions 2, 4, and 5) are measured. The Q-T interval and cycle length are measured in each cycle. An average is calculated for the respective measurements, and the Q-T interval is then corrected for heart rate according to Bazett's formula. Our own technique is less laborious, and our results are reproducible. However, in cases of doubt the method suggested by Taran and Szilagyi[12] might result in clearer differentiation. Our over-all experience suggests that the Q-T_c interval, carefully evaluated, may be an important aid in making the diagnosis of myocardial dysfunction in children. It may assist in the diagnosis of rheumatic fever, and, perhaps more important, it may aid in the very difficult diagnosis of low-grade or "subclinical" rheumatic activity.

The minimum requirements of a study which attempts to evaluate the Q-T_c interval as a diagnostic aid in acute carditis are the following: (*a*) observations must be made on a body of well-defined clinical material under such conditions that

12. Taran, L. M., and Szilagyi, N., cited by Eden, A.: The Measurement of the Electrical Systole (QT Interval) in Acute Rheumatic Heart Disease: A Survey of the Recent English Literature, Bull. St. Francis Sanatorium, Vol. 8, No. 3, 1951, p. 20.

repeated evaluations can be made under controlled circumstances for a prolonged period; (*b*) all variables other than carditis which affect the measurement must be considered, and (*c*) a standard and adequate technique of measurement must be employed. We believe that the variable results reported by other investigators are due to failure to satisfy one or several of these requirements.

SUMMARY

The Q-T_c interval was significantly prolonged in a high proportion (84%) of patients with active rheumatic fever.

The Q-T_c interval was prolonged in only a very small proportion of patients with inactive rheumatic fever, acute infections, and other diseases. The significance of the prolonged electrical systole found in these groups is discussed.

A case is presented to illustrate the clinical course, laboratory findings, and changes in the Q-T_c interval during an acute rheumatic episode.

The Q-T_c interval was found to be a sensitive diagnostic aid in detecting active carditis, provided an adequate technique of measurement is employed and all factors which affect the Q-T interval are evaluated.

Mrs. Noel Gray Lawson and Miss Caroline Gouverneur gave indispensable aid in obtaining the electrocardiograms and assembling the data. The staff of the Rochester Convalescent Hospital for Children gave active cooperation in this study.

260 Crittenden Blvd.

Case Reports

BILATERAL CONGENITAL CHOANAL ATRESIA IN NEWBORN

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CHOANAL atresia is an obstruction between the posterior nares (choana) and the pharynx. It may be unilateral or bilateral, complete or incomplete. When the atresia is bilateral and complete, any circumstance interfering with the entrance of air into the oropharynx will produce the symptoms of anoxia—irregular, rapid respiration and cyanosis. This occurs when the mouth is closed, when the infant is relaxed, as in sleep, during sucking, or with manual closing of the mouth. Crying opens the oropharynx, air enters the lung, and symptoms of respiratory embarassment clear. The impelling instinct for nasal respiration causes these recurring cycles.

In the newborn because of the presence of the cyanosis and dyspnea the condition may frequently be misdiagnosed as asphyxia neonatorum. It may be easily missed at autopsy examination of newborn infants unless pathologists routinely verify patency of the nares.

Congenital choanal atresia is rather rare. It was first reported by Otto,[1] in 1829. Hanckel,[2] in September, 1949, was able to collect 235 previously reported cases. Most pediatric textbooks mention the condition. In Caffey's "Pediatric X-Ray Diagnosis" [3] there is a roentgenogram similar to the one we obtained for this infant.

The following case is presented to call attention once again to this condition, to its similarity to asphyxia neonatorum, and to a discussion of aids in diagnosis.

REPORT OF A CASE

M. W., a white male infant, was normally delivered on Feb. 3, 1951, at full term after a normal pregnancy. The infant cried spontaneously, and color was good. Shortly after birth, however, it was noted that the respirations were rapid and irregular, and the child was cyanotic. However, when the infant cried, the duskiness disappeared and the color became good again. The birth weight was 7 lb. 6 oz. (3,300 gm.).

The infant was well developed, well nourished. Physical examination was negative except for a cardiac rate which varied between 200 and 220. The lungs were clear and the liver not enlarged. Tachycardia was suspected as the possible cause of the cyanosis and dyspnea, and digitalis, 0.05 mg., was administered intramuscularly, and the dose was repeated in four hours. The infant was placed in an incubator and oxygen administered.

From the Pediatric and Otolaryngologic Services, Lebanon Hospital.

1. Otto, A. W.: A Compendium of Human and Comparative Pathological Anatomy, translated by J. F. South, London, B. Fellowes, 1831.

2. Hanckel, R. W.: Bilateral Choanal Atresia: Report of Case in Infant and Review of Literature, Ann. Otol. Rhin. & Laryng. **58**:852 (Sept.) 1949.

3. Caffey, J.: Pediatric X-Ray Diagnosis: A Textbook for Students and Practitioners of Pediatrics, Surgery & Radiology, Chicago, The Year Book Publishers, Inc., 1945, p. 82.

The next morning, Feb. 4, the heart rate was 130, but the cyanosis and dyspnea persisted. The infant was transferred to the pediatric service at Lebanon Hospital.

On admission the patient was placed in an oxygen tent. The cyanosis and dyspnea did not improve. There would be some periods during which the respirations were comfortable and the color good, but for the most part there was considerable respiratory distress. A roentgenogram of the chest and an electrocardiogram were normal. The blood and urine were within normal limits.

The first day in the hospital a nurse attempted to pass a catheter through the nasal cavity to feed by gavage; this was unsuccessful, and the catheter was passed orally. A definite diagnosis was not made at this time, and it was believed that the symptoms were probably due to some cerebral disturbance. On Feb. 10 milk was seen in the left external auditory meatus after mouth feeding. The otolaryngological consultant reported a perforation of the right tympanic membrane. Both nasal cavities were filled with a thick, tenacious mucus which when cultured yielded Pseudomonas aeruginosa. The smear of the ear discharge revealed Gram-negative bacilli and staphylococci. Penicillin, sulfadiazine, and streptomycin were administered.

Fig. 1.—Lateral roentgenogram of the skull. Iodized oil in both nares does not pass into nasopharynx.

Another attempt was made to pass a nasal catheter to facilitate feeding. This was unsuccessful, and the otolaryngologists were asked to determine the patency of the nasal passages. Catheters were passed for a distance of 1½ in. (3.8 cm.) in each cavity, but no mention was made as to their appearance in the pharynx. The report from a direct laryngoscopy was "Epiglottis found to be firm and normal. Vocal cords normal in structure and motion. Normal laryngeal airway."

The next day a mild silver protein solution was placed in each nostril. When the brown color did not appear in the pharynx, another attempt to pass nasal catheters was made. It was definitely determined that some obstruction in the posterior nares was present. Iodized oil was placed in both nasal cavities, and roentgenography was done (Fig. 1). The report confirmed the catheter and colored-fluid findings of complete obstruction in the posterior choanae.

On the 17th day the cyanotic spells became more frequent and more intense. A tracheotomy was performed. There was some improvement in breathing through the tracheotomy tube, but 36 hours later the patient again became cyanotic and dyspneic and died.

Autopsy Findings.—Anatomical Diagnosis: The anatomical diagnoses were (1) congenital choanal atresia, bilateral; (2) status 36 hours after tracheotomy; (3) pneumothorax, left; atelectasis, left lung; (4) mucopurulent tracheobronchitis, diffuse; (5) emphysema and focal hemorrhages, right lung; (6) bronchopneumonia, focal; (7) purulent otitis media, left.

Cause of Death.—The cause of death was bronchitis and pneumothorax.

Ears: There was abundant purulent exudate in the left middle ear. Smear showed pus cells, no organisms. The left tympanic membrane was perforated. The right middle ear contained no exudate.

Respiratory System: The nasal cavities contained abundant mucus. A probe could be passed into each nostril for 1½ in., at which point it encountered a complete obstruction of the choanae, bilaterally. When the choanae were viewed posteriorly, from the nasopharynx, a small dimple was seen from either side of a median septum, ending blindly. The obstruction appeared bony. There were no other anomalies of the upper respiratory tract, including the larynx. At the level

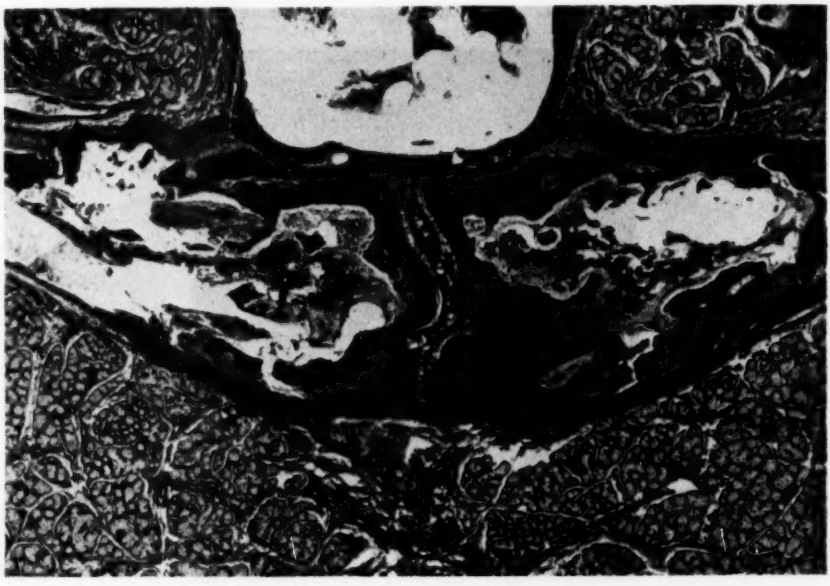

Fig. 2.—Frontal section through the bony plates obstructing the choanae. A midline fibrous septum separates the two symmetrical plates. Below are mucous glands of the soft palate.

of the second and third tracheal rings there was a small incision in the anterior wall of the trachea. There was no obstruction in the region of this incision. Below the level of the tracheotomy, the lumen of the trachea was filled with a reddish mucoid material. The mucosa of the tracheobronchial tree was pale pink. The pleura were smooth and shiny throughout. The left lung was for the most part airless, except for small parts of the upper lobe. The lower lobe was pale and fleshy. The upper lobe showed multiple patches of dark red color. There was no evidence of interstitial emphysema in the left lung. The right lung was voluminous and showed the usual number of lobes. The surface of the right lung had a strikingly mottled appearance, and the lobular architecture was very distinct. Groups of lobules were dark red, while others had a pale pink color. The upper lobes were fairly well aerated, while the lower lobe contained little air. The lung parenchyma was heavy and wet, and frothy fluid could be expressed from the cut surface. A culture taken from the right lower lobe was sterile. The mouth and oropharynx showed no abnormalities. The tongue was not unusual in size and shape. The soft palate and uvula were normally formed. The remainder of the organs showed no malformations or anomalies. A section through the atresia is shown in Figure 2.

COMMENT

Congenital atresia may be unilateral or bilateral. The unilateral type is more frequent than the bilateral type. It may be complete or incomplete. The incomplete type is rarely diagnosed, for it causes little obstruction and few symptoms. The structure of the obstructing wall may be membranous or osseous or membrano-osseous. According to Schwartz and Isaacs,[4] the thickness of the occluding bony structure may be as great as 12 mm.

The primary symptom of congenital choanal occlusion is the inability to breathe through the affected nostril. When in the newborn infant both sides are occluded, it becomes an emergency problem. When respiratory difficulty, cyanosis, and dyspnea are presented, an immediate investigation of the patency of the posterior choanae should be undertaken. Passage of an infant's size rubber nasal catheter through the nose into the nasopharynx is the simplest method. This should be done on both sides. If the catheter does not pass, mild silver protein, or other colored fluid, can be instilled in the nares. If the colored fluid appears in a case in which the catheter cannot pass, a partial obstruction (incomplete) can be assumed. If the colored fluid does not pass, the diagnosis of complete obstruction may be confirmed by roentgenography after instillation of opaque oil. A probe may be useful in determining the character of the obstructing structure.

Unilateral choanal occlusion may pass unnoticed for years. It presents no emergency problem. If the condition is undiagnosed in infancy, the following may suggest nasal obstruction: (*a*) history of inability to breathe through affected side; (*b*) history of feeding problem in infancy; (*c*) thick, tenacious mucus in the affected nostril; (*d*) anosmia; (*e*) a high-arched palate on the occluded side or both sides; (*f*) nasal septum deviated to the side of the atresia; and, (*g*) patient a mouth breather and the upper incisors irregular.

The several theories as to the development of the congenital occlusions are reviewed by Hanckel [2] and Boyd.[5] The most frequently accepted theory is that of the persistence of the bucconasal membrane. Schaeffer [6] described the formation and disappearance of the membrane. The persistence of the buccopharyngeal membrane or the overgrowth of the vertical and the horizontal palatal processes are the two other possible causes.

TREATMENT

Many forms of treatment have been advocated. These range from simply breaking through the obstruction and following this with removal of the remaining wall and posterior border of the vomer by biting forceps to a transpalatal approach first advocated by Brunk [7] in 1909, modified by Schweckendiek [8] in 1937 and by

4. Schwartz, A. A., and Isaacs, H. J.: Congenital Atresia of the Posterior Nares, Report of 2 Cases, Arch. Otolaryng. **35**:603 (April) 1942.

5. Boyd, H. M. E.: Congenital Atresia of the Posterior Nares, Descriptions of Technics Used in Meeting Operative Difficulties and Report of Case, Arch. Otolaryng. **41**:261 (April) 1945.

6. Schaeffer, J. P.: Various Types of Congenital Atresias of the Nose and Their Genetic Interpretation, Tr. Am. Laryng. A. **56**:126, 1934.

7. Brunk, A. A.: New Case of Unilateral Osseous Choanal Occlusion: An Operation Through the Palate, Ztschr. Ohrenh. **59**:221, 1909.

8. Schweckendiek, H.: Transpalatal Therapy of Congenital Choanal Atresia, Ztschr. Hals-, Nasen- u. Ohrenh. **42**:367, 1937.

Ruddy [9] in 1945. The choice of operation is dependent on the type of pathologic changes. In unilateral occlusion unless malformation of the face is evident, operation may be postponed until the patient is old enough to withstand the trauma of the procedure and the postoperative care.

In bilateral complete choanal occlusion if the symptoms are mild, operation may be postponed until the patient is 9 months old (Geiger and Roth [10]), or, according to Richardson [11] and to Cinelli,[12] to the age of 2 years. The fact that some patients with complete bilateral occlusion survive to adult life has been noted by Boyd [5] and Klaff.[13] However, when symptoms are severe, no postponement of the operation is possible. Hanckel [2] was able to delay operation on his patient until the 41st day of life, but a tracheotomy had to be performed when the patient was 1 month old to relieve the dyspnea at feeding. In our case the child died 36 hours after tracheotomy before any surgery could be performed to the postnasal occlusion.

The otitis media of the left ear was due to the regurgitation of milk through the Eustachian tube, with resultant middle ear infection.

SUMMARY AND CONCLUSIONS

A case of congenital atresia of the choanae in a newborn infant is presented.

Several diagnostic criteria and methods are mentioned.

More thorough autopsy examination in cases of asphyxia neonatorum might reveal hitherto undiagnosed cases of choanal atresia.

Routine examination to determine patency of the choanae should be performed in all cases of tonsillectomy and adenoidectomy.

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9. Ruddy, L. W.: Transpalatine Operation for Congenital Atresia of the Choanae in Small Child or Infant, Arch. Otolaryng. **41**:432 (June) 1945.

10. Geiger, C. W., and Roth, J. H.: Osseous Choanal Obstruction and Adenoid Tissue, Arch. Otolaryng. **15**:441 (March) 1932.

11. Richardson, C. W.: Congenital Occlusion of the Post-Nasal Orifices, with Report of a Case, Tr. Am. Laryng. A. **35**:226, 1913.

12. Cinelli, A. A.: Nasal Atresias: A Surgical Critique, Ann. Otol. Rhin. & Laryng. **49**:912 (Dec.) 1940.

13. Klaff, D. D.: Bilateral Congenital Atresia of the Choanae, Arch. Otolaryng. **41**:298 (April) 1945.

COR TRILOCULARE BIATRIATUM WITH TRANSPOSITION OF LARGE VESSELS

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AMONG congenital cardiovascular defects, transposition of the great arteries is one which is infrequently found, and it is found more frequently in boys than in girls.[1] The survival period will be short unless the defect is combined with septal defects and a patent ductus arteriosus. In Abbott's series of 1,000 patients with congenital cardiovascular defects, 74 showed complete transposition of the aorta and pulmonary artery, but in only 49 was it the primary defect. In 32 of these 49 patients no septal defects existed, while in 17 transposition was combined with an interauricular or interventricular septal defect.

Mannheimer [2] found among his 114 cases of morbus caeruleus six patients with transposition of the great vessels with cyanosis at birth; in four patients fits of cyanosis and dyspnea occurred, and five died before the age of 4 months. Polycythemia and clubbing of the fingers and toes generally do not occur in the short survival period before death. In four of five cases a defect of the interventricular septum existed, and in three patent foramen ovale and patent ductus arteriosus were present. Clinically there seemed to exist a parallelism between present septal defects and a harsh systolic heart murmur. Typical signs were progressive cardiac enlargement, a narrow vessel trunk in the anteroposterior roentgenogram with the trunk wider in the lateral view, and increased pulmonary pulsation.

Lichtenstein,[3] in Fanconi and Wallgren's "Lehrbuch der Pädiatrie," writes about cor triloculare as an infrequent malformation and mentions that survival in cases of transposition of the large vessels may be for a few months only. Taussig [4] gives in her "Congenital Malformations of the Heart" the most extensive description about transposition, including auxiliary defects which may be present. The etiology of transposition is obscure, but the general opinion is that it is a developmental error.[5] In complete transposition we find the aorta arising from the right ventricle and the pulmonary artery from the left one. When the interauricular and interventricular septums remain intact, this malformation is not compatible with life. A patent ductus arteriosus either alone or in combination with septal defects plays a vital role. Before birth no circulatory disturbances are to be feared, but for extrauterine existence a crossing over between the two circulations must be present to provide the complete circulation with oxygenated blood. In cases of intact septums

1. White, P. D.: Heart Diseases, Ed. 3, revised, New York, The Macmillan Company, 1947, p. 308.

2. Mannheimer, E.: Morbus Caeruleus, New York, S. Karger, 1949, pp. 226 and 294.

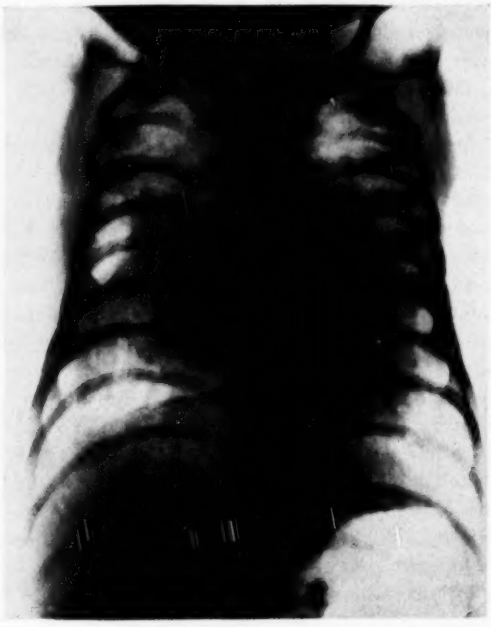
3. Lichtenstein, in Fanconi, G., and Wallgren, A.: Lehrbuch der Pädiatrie, Basel, Benno Schwabe & Co., 1950, p. 591.

4. Taussig, H. B.: Congenital Malformations of the Heart, London, Commonwealth Fund, 1947, p. 197.

5. Brown, J. W.: Congenital Heart Disease, Ed. 2, New York, Staples Press, Ltd., 1950, pp. 250-270.

cyanosis will be present from birth; a patent ductus arteriosus and septal defects will function depending on pressure in the left and right sides of the heart, giving only slight cyanosis during crying or nursing. Gradually cyanosis deepens, and clubbing may develop; failure to gain weight is common. Usually a harsh systolic murmur will be heard over the enlarged heart outline, but a diagnosis may be possible after roentgenography. In the anteroposterior position the vessel trunk is narrow with an absence of the fullness of the conus pulmonalis; circulatory engorgement of the interstices is common. The electrocardiogram shows no more than right axis deviation.

When transposition is combined with septal defects, the child can be acyanotic at birth, and he may be discharged as a normal baby. Later cyanosis will appear,



Enlarged heart shadow.

with clubbing depending on length of survival time and intensity of cyanosis, and general prognosis is poor.

REPORT OF A CASE

A. S., the third child, a boy, of healthy parents, was born prematurely. The mother had toxemia with high blood pressure during the pregnancy and lived from the second month on a salt-poor diet. The parturition started three weeks before the calculated end of pregnancy, but birth was quite normal, and the baby cried immediately. The mother, from her experience with the two other children, thought the "respiration" a little abnormal, especially after nursing, but the doctor in charge released the mother and child after 10 days. In spite of this, the mother was anxious about the baby's weight; she thought the baby was too short of breath to drink sufficiently and that this was the reason for lack of increase in weight. Motions, however, were quite normal. Body temperature always remained too low, usually was not more than 36 C. (96.8 F.).

At 3 weeks of age the general condition was so poor that hospital care seemed necessary. He was then a very dystrophic child with a body weight of 2,700 gm. and with pyoderma; muscle tone was lacking, and the child was very cyanotic and short of breath. The heart outline was too large to the left and to the right on percussion (Figure). A very harsh systolic murmur was heard to the left side of the sternum in the fourth intercostal space, while in the region of the pulmonary artery a very long-lasting machinery murmur could be heard. The second pulmonary sound was too loud. The liver was enlarged. The whole thorax was in extreme inspiration, and on auscultation a shower of moist rhonchi could be heard over both the lungs. The pulse rate was 140, regular, but very weak; blood pressure was low. There was a high hemoglobin content (17 gm.) and the red blood cell count was 5,000,000. On the anteroposterior roentgenogram, in contrast to the lateral roentgenogram, a very narrow vessel trunk, an enormously enlarged heart, overfilling of the interstices, and low lung borders because of emphysema were shown.

The child received therapy—oxygen tent, stimulants—but died within 24 hours with increasing signs of heart decompensation. The clinical diagnosis was transposition of the large vessels with patent ductus arteriosus and ventricular septal defect.

Partial autopsy was permitted. Besides the extremely poor nutritional condition, there was found a liver enlarged by heart decompensation and a spleen only slightly enlarged. All over the stomach and the intestines capillaries were distended with blood. The lungs were slightly emphysematous. The heart was very large—equal in size to more than the two fists of the baby together—and was especially enlarged toward the right. When the ventricles were opened, it was found that they were continuous; the whole interventricular septum was lacking; the tricuspid and mitral cusps were intact. The aorta and pulmonary artery were in transposition, but both vessels arose from the common ventricle. The aorta was lying before the pulmonary artery and was less in circumference, 12 mm.; the cusps and coronary arteries were normal. The aortic arch was lying to the right of the trachea, crossing over the right main bronchus. The ductus arteriosus was patent but had a rather narrow lumen. The pulmonary artery presented a widening of the lumen between the origin in the heart and the branching into the right and left lung arteries; the lumen reached 20 mm. in circumference. The caval veins brought the venous blood normally back into the right atrium, which had a distinctly hypertrophic wall with dilatation. The left atrium was much smaller and had a thinner muscular wall. The foramen ovale had a large patent opening 1 cm. in cross section. The pulmonary veins were engorged with blood.

After autopsy the clinical diagnosis was corrected to cor triloculare biatriatum, transposition of the large vessels, patent ductus arteriosus, and patent foramen ovale. The widening of the pulmonary artery between ventricle and branching of right and left pulmonary artery resembled the conus pulmonalis described in Eisenmenger's complex and in Taussig's syndrome (Third Inter-American Congress of Cardiology, 1948).[6]

SUMMARY

A 3-week-old boy suffered from congenital cardiovascular defects consisting of transposition of the large vessels, patent ductus arteriosus, patent foramen ovale, and lack of interventricular septum. Cyanosis occurred two weeks after birth; clubbing did not occur in the short time before death.

6. van Buchem, F. S. P.; van Wermeskerken, J. L., and Orie, N. G. M.: Transpositie van de aorta: Het syndroom van Taussig, Nederl. tijdschr. geneesk. **94**:873, 1950.

Progress in Pediatrics

TICK PARALYSIS ON THE ATLANTIC SEABOARD

Study of Incidence During Poliomyelitis Season with Report of a Case and Review of Published Cases

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TICK PARALYSIS is an acute disease of the central nervous system with symptoms ranging from weakness of the legs and ataxia to paralysis of all four limbs, and, in severe cases, as the disease advances, to bulbar paralysis closely simulating anterior poliomyelitis. It is flaccid and ascending in character (Landry type). Its occurrence at the peak of tick infestation coincides with the poliomyelitis season, making its recognition imperative. It is still rare but becoming more prevalent in the Eastern Seaboard States, as the added cases being reported from year to year indicate.

It can be fatal, death being due to involvement of the cranial nerves with ultimate respiratory paralysis, and since death may be prevented when the disease is recognized early by the simple removal of the tick, it is essential that the physician be aware of the existence of such a syndrome, especially in tick-infested areas. The dramatic improvement which follows the removal of the tick has been exemplified in the 23 cases thus far reported in the East, since only one patient died.

Only since 1938 has tick paralysis been reported as occurring in the States east of the Rockies. The 23 cases found have been distributed as follows: Colorado,[1] one; Georgia,[2] seven; Idaho,[3] one; Kentucky,[4] two; New York,[5] one; North Carolina,[6] one; Pennsylvania,[7] one; South Carolina,[8] three; Texas,[9] one; Virginia,[10] five.

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1. Amesse, J. W., and Lyday, J. H.: Tick Paralysis in Colorado, Rocky Mountain M. J. **36**:640 (Sept.) 1939.

2. (*a*) Robinow, M., and Carroll, T. B.: Tick Paralysis Due to Bite of American Dog Tick: Report of Case Observed in Georgia, J. A. M. A. **111**:1093 (Sept. 17) 1938. (*b*) Mulherin, P. A.: Ataxia Due to Bite of American Dog Tick (Dermacentor Variabilis Say), J. Pediat. **16**:86 (Jan.) 1940. (*c*) Harper, A.: Tick Paralysis: Report of a Case, J. M. A. Georgia **31**:442 (Dec.) 1942. (*d*) Ransmeier, J. C.: Tick Paralysis in the Eastern United States, J. Pediat. **34**:299 (March) 1949.

3. Barnett, E. J.: Wood Tick Paralysis in Children, J. A. M. A. **109**:846 (Sept. 11) 1937.

4. Prince, G. E.; Keeley, J. C., and Scott, E. P.: Tick Paralysis in Children, J. Pediat. **28**:597 (May) 1946.

5. DeSanctis, A. G., and di Sant'Agnese, P. A.: Tick Paralysis: Report of Case in New York, J. A. M. A. **122**:86 (May 8) 1943.

6. Townsend, R. G., and Nash, J. F.: On Certain Diseases from the Fields and Woods, South. Med. & Surg. **102**:386, 1940.

7. Dawson, K. E.; Sherman, A. J., and LaBoccetta, A. C.: Tick Paralysis: Report of Case in Philadelphia, Am. J. Dis. Child. **79**:491 (March) 1950.

8. Gibbes, J. H.: Tick Paralysis in South Carolina, J. A. M. A. **111**:1008 (Sept. 10) 1938. Beach, M. W., and Ravenel, B. O.: Tick Paralysis in South Carolina, J. South Carolina M. A. **37**:323 (Dec.) 1941. Ryan, C. P., and Canning, H. B.: Tick Paralysis Resulting from Infestation with Dermacentor Andersoni of Stiles, the Common Rocky Mountain Wood Tick, ibid. **40**:229 (Nov.) 1944.

In 1948 McCue, Stone, and Sutton [10a] tabulated the 13 cases which had occurred in the literature until 1946. Of these, in three cases respiratory paralysis had developed. A similar summary of the cases which have been reported since is shown in the table. As noted, of the 10 cases, in four signs of bulbar involvement developed, two with respiratory paralysis.

HISTORY

Abbott,[11] in 1943, and Stanbury and Huyck,[12] in 1945, reviewed the literature and reported that in 1824 William Howell, in Australia, stated that the tick would in the end "destroy man or beast if not removed in time." In 1843 Backhouse, in Australia, described the destruction of sheep, foal, and calves, paralysis of the hindlegs often preceding death. In 1884 Bancroft, in Queensland, observed weakness of the hindlegs of dogs and cats two or three days after attachment of the tick, with consequent death of the animal, except occasionally when the tick was removed. In 1894 Anderson and Stewart, in New South Wales, described paralysis in dogs with ticks. In 1904 Malley, in South Africa, described paralysis and death in sheep. In 1905 Borthwick described the same in Cape Colony. In 1912 Todd first recognized the disease as occurring in man in North America. He cited Temple in British Columbia as first describing it, in 1896.

ETIOLOGY

Bacterial and viral agents have been suspected. The accepted theory, however, is that tick paralysis is due to a toxic agent produced by the tick. Sabbatani,[13] in 1898, while studying the anticoagulant factors of tick salivary secretion, observed paralysis in experimental animals following the intravenous injection of emulsified ticks. Hadwen,[14] in 1913, concluded that "the most likely explanation seems to be that the paralysis is due to the toxins inoculated by the ticks and that these are elaborated especially at the time when gorging is rapid; i. e., 24 hours or so before the ticks drop off. The average time six females took to gorge was 6½ days."

9. Bloxsom, A., and Chandler, A. C.: Transient Paralysis Due to Bite of American Dog Tick (Dermacentor Variabilis Say), Am. J. Dis. Child. **67**:126 (Feb.) 1944.

10. (*a*) McCue, C. M.; Stone, J. B., and Sutton, L. E., Jr.: Tick Paralysis: 3 Cases of Tick (Dermacentor Variabilis Say) Paralysis in Virginia, with a Summary of All the Cases Reported in the Eastern United States, Pediatrics **1**:174 (Feb.) 1948. (*b*) Stiller, R.: Tick Paralysis: Case Report, Clin. Proc. Child. Hosp. **2**:266 (Sept.-Oct.) 1946. (*c*) Randolph, M. F.: Tick Paralysis: Report of 2 Cases, Clin. Proc. Child. Hosp. **3**:278 (Oct.) 1947.

11. Abbott, K. H.: Tick Paralysis: A Review, Proc. Staff Meet., Mayo Clin. **18**:39 (Feb. 10); 59 (Feb. 24) 1943.

12. Stanbury, J. B., and Huyck, J. N.: Tick Paralysis: Critical Review, Medicine **24**:219 (Sept.) 1945.

13. Sabbatani, L.: Fermento anticoagulante dell' Ixodes Ricinus, Gior. Accad. med. di Torino **4**:380, 1898; Arch. ital. biol. Turin **31**:37, 1899; cited by Nuttall, G. H. F., and Strickland, C.: On the Presence of an Anticoagulin in the Salivary Glands and Intestines of Argas Persicus, Parasitology **1**:302, 1908.

14. Hadwen, S.: On "Tick Paralysis" in Sheep and Man Following Bites of Dermacentor Venustus, with Notes on the Biology of the Tick, Parasitology **6**:283, 1913.

Cases of Tick Paralysis Reported Since 1946

Source	Location	Date	Patient		Tick	Neurological Findings	Bulbar Paralytic Changes	Hr. Before Improvement Noted After Tick Removal	Days Before Complete Recovery After Tick Removal
			Age, Yr.	Sex					
McCue, Stone, and Sutton [10a]	Virginia	7/47	9	F	D. variabilis Say, female	Weakness of all extremities; weakness of back; hyperesthesia	5 days after onset of symptoms, lateral nystagmus, poor phonation, slight difficulty in swallowing, respiratory difficulty (respirator used)	"Few"	3
	Virginia	?	10	F	Engorged; tick not saved	Ataxia; paralysis of legs; weakness of arms and back	None	12	6
	Virginia	3/45	1½	M	Partially engorged, not identified	Paralysis of legs and arms; weak neck muscles	4 days later, difficult swallowing	9	1
Ransmeier [2d]	Georgia	5/48	3	F	Unidentified	Paralysis of legs; weak arms and neck	2 days later, thick speech, difficult swallowing, respiratory paralysis (oxygen nasally)	9	4
	Georgia	5/48	4	F	Unidentified	Weakness of legs; ataxia	None	10	½+
	Georgia	6/48	6	F	D. variabilis Say; ova deposited after detachment	Weak legs; ataxia; hyperesthesia of legs	None	22	6
	Georgia	7/48	2	M	D. variabilis Say	Weak legs; ataxia	None	12	3½+
Dawson, Sherman, and La Boccetta [7]	Pennsylvania	7/48	9	F	D. variabilis Say, sex?	Weak legs; generalized weakness; ataxia; paresthesia	2 days later, thick speech, left facial palsy	24	7
Stiller [10b]	Virginia	7/46	2½	F	D. andersoni Stiles, female	Weak legs; weak neck and back; ataxia of arms	None	Gradual	12
Randolph [10c]	Virginia	6/47	3½	F	Identification unreported	Weak legs, back, and arms; ataxia; nuchal rigidity	None	1	1

Gregson [15] in his experiments concluded also that the greatest amount of toxin was elaborated between the fifth and seventh days of attachment. Dodd,[16] in 1921, produced paralysis and death in a guinea pig and a dog six to nine days after attaching unengorged female ticks.

Hadwen and Nuttall,[17] in 1912, reproduced paralysis in a dog after attachment of a tick. They also studied the effect of larvae and nymphs on guinea pigs and from their experiments concluded that whereas larvae and nymphs could produce death of the guinea pig between the fifth and seventh days of attachment, the resultant adults produced no pathogenic effects. At that time they could not explain the deaths of the guinea pigs, since this had been attributable only to toxins derived from adult female ticks. Regendanz and Reichenow,[18] in 1931, carried the above experiments further. They injected saline emulsions of tick ova subcutaneously and intraperitoneally in dogs, guinea pigs, rats, mice, rabbits, and canaries, producing weakness of the extremities 3 to 24 hours later with death in the majority of the animals. Their conclusions can be summarized as follows:

1. The toxin is produced by the tick during maturation of the eggs, and the greatest accumulation of the toxin is concentrated in the ovaries and eggs.

2. The more mature the eggs, the greater the amount of toxin present.

3. After the eggs are laid, only a small amount of toxin is demonstrable in the rest of the tick (as in salivary glands, head glands, and Malpighian bodies).

4. The capsule coating of the egg contains no toxin.

5. As the eggs develop into larvae, the larvae contain progressively less toxin, presumably broken down by the metabolism of the growing larvae.

6. This toxin is either produced or concentrated in the ova of the gravid tick.

(It is apparent that only fertilized eggs were used in the aforementioned experiments, which could account for the failure of other observers to duplicate the results.)

Ross,[19] in 1926, injected emulsified salivary glands of engorged female ticks into white mice, producing stiffness and difficult gait in one hour, but this could not be reproduced in guinea pigs or dogs, even with intravenous injection. Steinhaus,[20] in 1942, killed guinea pigs regularly with the filtrate of triturated eggs of Dermacentor andersoni.

McCornack,[21] in 1921, allowed the tick removed from an affected child to attach itself to a guinea pig, which caused the death of the animal six days later. Prince,

15. Gregson, J. D.: Studies on the Rate of Tick Feeding in Relation to Disease, Proc. Soc. Entomol. Brit. Columbia, No. 33, p. 15, Jan. 1937.

16. Dodd, S.: Tick Paralysis, J. Comp. Path. & Therap. **34**:309, 1921.

17. Hadwen, S., and Nuttall, G. H. F.: Experimental "Tick Paralysis" in the Dog, Parasitology **6**:298, 1913.

18. Regendanz, P. V., and Reichenow, E.: Ueber Zeckengift und Zeckenparalyse, Arch. Schiffs- u. Tropen-Hyg. **35**:273 (May) 1931.

19. Ross, I. C.: An Experimental Study of Tick Paralysis in Australia, Parasitology **18**: 410, 1926.

20. Steinhaus, E. A.: Note on a Toxic Principle in Eggs of the Tick, Dermacentor Andersoni Stiles, Pub. Health Rep. **57**:310 (Aug. 28) 1942.

21. McCornack, P. D.: Paralysis in Children Due to the Bite of Wood Ticks, J. A. M. A. **77**:260 (July 23) 1921.

Keeley, and Scott [4] in one of their cases, in 1945, reported that the tick which had been removed intact from their patient laid eggs seven days after detachment. An extract of these eggs injected into a white mouse caused paralysis and death; the control mouse survived. (There should be no doubt that the eggs contained a toxin, excretable through the saliva, which was responsible for this syndrome in that patient.)

On the basis of the above findings, it has been postulated that the toxin can be excreted only by a "gravid" female. In only two of the investigations (Hadwen and Nuttall [17] and Regendanz and Reichenow [18]) were known fertilized eggs used; the state of fertilization is not explained in the experiments of the others. Unfortunately, the same doubt exists in this series of 23 cases thus far reported in human beings, inasmuch as the tick was unidentified as to species in 10 cases, was definitely identified as "female" in 10 cases, and was identified as "pregnant female" in only 3 cases,[22] however, with the status of fertilization unknown in these 3 cases.

Bow and Brown [23] were the only ones to report a case of partial paralysis of the arm which cleared up after the removal of a male tick. This is not in accordance with the findings of all other writers, either in the laboratory or in clinical fields.

DISTRIBUTION OF TICKS

The cause of the disease in the West is the Western wood tick, D. andersoni Stiles; in the East and Central states the very common dog tick (also called Eastern wood tick), D. variabilis Say, is more frequently concerned. In the 23 cases thus far reported in the East, 4 cases were due to D. andersoni (one of which was not positively identified); 10 cases were due to D. variabilis, and 9 were of unknown cause.

The wood tick, according to Bishopp and Trembley,[24] is found in the states west of the Rockies (Washington, Idaho, Wyoming, Oregon, California, Nevada, Utah, Colorado, New Mexico, and Arizona), also in Nebraska and South Dakota.

The dog tick is much more widely distributed, being found in all the states except Washington and the Rocky Mountain and Intermountain States (Idaho, Wyoming, Nevada, Utah, Colorado, Arizona, and New Mexico). It is concentrated on the Atlantic Seaboard, in localities with high humidity and particularly on Long Island and Cape Cod. (Figs. 1 and 2).

The dog tick undergoes four stages in its life cycle: the egg, the larva or seed tick, nymph, and adult. Whereas the young ticks feed upon small wild animals, the meadow mouse being the principal host, the adult ticks prefer dogs and larger wild animals, such as rabbits, squirrels, foxes, and racoons. They also infest horses, cattle, and hogs. Man is frequently bitten but is not a preferred host.

Ticks are found to be abundant in damp areas covered with underbrush, tall grass, and weeds. Beach grass and grassy patches in woodland are also favored.

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22. Ransmeier.[2d] Prince, Keeley, and Scott.[4] DeSanctis and di Sant'Agnese.[5]

23. Bow, M. R., and Brown, J. H.: Tick-Borne Diseases of Man in Alberta, Canad. M. A. J. **53**:459 (Nov.) 1945.

24. Bishopp, F. C., and Trembley, H. L.: Distribution and Hosts of Certain North American Ticks, J. Parasitol. **31**:1 (Feb.) 1945.

They are seldom found in forests, unless these areas have been denuded in lumbering.

The adult ticks are attracted to the edges of paths. Experiments have shown that they are attracted by the scent of animal odors (dog or man).[25] They are concentrated in these areas, lurking on the edges of grass, prepared to attach themselves immediately to a passing host which brushes against them.

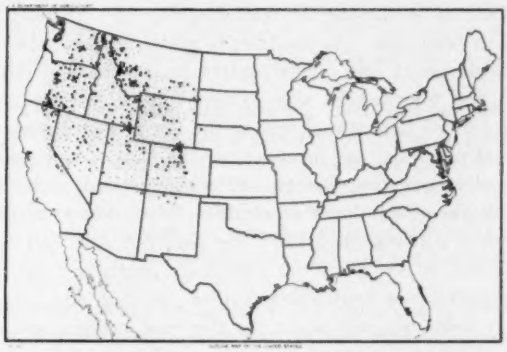

Fig. 1.—Distribution map for D. andersoni: Large dots indicate localities from which specimens were reported; small dots indicate probable locations (published with the permission of the United States Bureau of Entomology and Plant Quarantine).

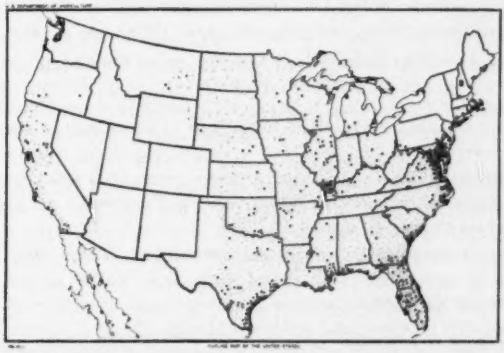

Fig. 2.—Distribution map for D. variabilis: Large dots indicate localities from which specimens were reported; small dots indicate probable locations (published with the permission of the United States Bureau of Entomology and Plant Quarantine).

SEASONAL OCCURRENCE AND INCIDENCE

The tick season starts in March and ends in August, May through July being the peak of tick infestation. The majority of the cases reported have been in June and July. This overlaps the usual poliomyelitis season, making differential diagnosis imperative.

25. Smith, C. N.; Cole, M. M., and Gouck, H. K.: Biology and Control of American Dog Tick, Technical Bulletin 905, U. S. Department of Agriculture, Bureau of Entomology and Plant Quarantine, 1946.

It has been stated that tick paralysis is commoner in children than in adults, the ratio being 10:1. Of the 23 cases reported, 1 occurred in a woman, 19 in girls, and 3 in boys.

DIAGNOSIS

The clinical picture which has been described [26] shows practically no difference from that originally portrayed by Temple [27] in 1912. The patient, usually a girl between the ages of 3 and 10 years, may be slightly irritable one day, may go to bed feeling well, and on awakening the following day may complain of some pain or numbness in one or both legs. As she tries to get out of bed, she may fall because of stiffness or weakness of legs. She prefers to stay in bed, but may go to the breakfast table. She may not be able to feed herself because of incoordination. Within the next 4 to 24 hours weakness of the lower extremities has increased to the stage of flaccid paralysis, and weakness of the back muscles will be present so that the child can no longer sit up but will fall if unsupported, in the same fashion as a "rag doll." Weakness of the upper extremities, advancing to actual paralysis, will occur. If the tick is still not discovered, the paralysis may ascend, speech will be mumbled, the patient is conscious but extremely apathetic; she cannot talk; she cannot move; deglutition is next affected, then the face and ocular muscles, and finally respiratory paralysis will occur, as the vital centers are affected.

There is an early and symmetrical loss of all deep reflexes; the superficial reflexes may be maintained. No abnormal reflexes are usually present, though stiffness of neck and back have been reported.

In the milder cases there may be only slight weakness of the extremities, with a cerebellar type of ataxia as the predominant neurological finding.

The spinal fluid, hemogram, temperature, and pulse are all normal.

Diagnostic Points.—The following diagnostic points are seen in the development of tick paralysis:

1. Sudden onset of afebrile asthenia, with or without localized pain in the lower extremities, which, however, is never severe.
2. Early and symmetrical losses of all deep reflexes. Superficial reflexes may be maintained in the ataxic type. Signs of meningeal irritation (Kernig, Brudzinski) are rare.
3. Clear sensorium with marked apathy.
4. Ascending flaccid paralysis, complete and symmetrical, which may ultimately end in bulbar paralysis.
5. Ataxia, paresthesia may occur.

Differential Diagnosis from Poliomyelitis.—The following points aid in distinguishing tick paralysis from poliomyelitis:

1. Absence of fever.
2. Relatively painless ascending paralysis which is symmetrical and flaccid.
3. Entirely normal spinal fluid.
4. Absence of significant pain or spasm in any particular muscle group.
5. Loss of all deep reflexes very early in the disease even before paralysis becomes apparent.
6. Picture of extreme apathy.
7. History or finding of a tick or bite.

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26. Abbott.[11] Stanbury and Huyck.[12]

27. Temple, I. U.: Acute Ascending Paralysis, or Tick Paralysis, Med. Sentinel **20**:507, 1912; cited by Nuttall, G. H. F.: "Tick Paralysis" in Man and Animals, Parasitology **7**:95, 1914.

REPORT OF CASE

R. M. W., a 3½-year-old white girl from Bedford Hills, N. Y., was admitted to the Northern Westchester Hospital on July 25, 1950, at 1:30 p. m. with complaints of headache, pain behind the right knee, and inability to walk because of pain and weak legs. Two days before she had fallen down a bank, landing on her head on a concrete pavement. She cried immediately and had no ill effects except for vomiting of supper one hour later. She acted normally until 4 a. m. of the day of admission, when she woke up with pain behind the right knee and fell asleep again. She woke up at 7 a. m. with headache and pain behind the knee, tried to get out of bed but fell down because of weak legs. She remained in bed until admission, refused solids but took water well. On admission she had a headache and pain in the legs only on active motion.

She had not been out of town. She had a dog of her own, and there were other dogs in her neighborhood.

Past History.—No previous illnesses were reported. There were nine siblings, all well.

Physical Findings.—July 25: On this day, of admission, at 1:30 p. m., a well-nourished, well-developed 3½-year-old girl in tears and moderately lethargic was seen. She tended to remain motionless; the eyes occasionally became fixed but followed objects well. The physical examination gave negative results except for the neurological findings: there was no nuchal resistance, but she had difficulty in holding up her head, and when sitting up she used her arms to support herself. The cranial nerves showed no abnormality. All deep reflexes were hypoactive. She was clear, oriented, and cooperative.

At 7 p. m. all deep reflexes except the brachialis (2+) were absent; Kernig and Brudzinski signs were not seen. All abdominal reflexes were present weakly. The neck was supple to extreme flexion. There was no muscle spasm, but marked flaccidity of the muscles of the neck, back, and lower extremities was seen. In the sitting position the head could be flexed to the point of touching the forehead to the toes of the extended legs (limp "rag doll" appearance). She could move her legs and arms spontaneously without any incoordination. She preferred to lie quietly in bed. She was made to walk, took three steps supported by the axillae, then collapsed, and complained of pain behind the left knee.

July 26: During the night, according to the nurse's report, she slept quietly. At 3 a. m. she shook the side of the crib and cried. She was very apathetic, stared, and blinked often. She shook all over when she tried to sit up. At 4 a. m. she asked for the bed pan, sat on it; but her head drooped limply, and she complained to the nurse of "pain in back of the neck." She refused to stay covered. Between 5 and 9 a. m. she slept at intervals, whining when awake. From 9 to 10 a. m., she became increasingly lethargic.

At 10 a. m. an engorged tick was found in the left frontotemporal region of the scalp and removed. By 11 a. m. she could not talk and also had difficulty in swallowing. Physical examination at that time revealed the child to be lethargic but not in coma, with eyes open and fixed, lids blinking often, and with mouth open. When she was disturbed or stimulated by a pin, there was a muffled cry, but she did not move. Both legs could still be moved spontaneously, although moderately. Both arms showed complete flaccid paralysis. The gag reflex was present, with accumulation of secretions in the pharynx and drooling and gurgling. All reflexes were absent, including the abdominal. Complete flaccid paralysis of neck, trunk, and arms and moderate flaccid paralysis of the lower extremities were present. Respiration was normal, but since speech loss and pharyngeal paralysis had appeared and were becoming rapidly progressive two hours after removal of the tick, it was considered safest to transfer the child to the poliomyelitis center at Grasslands Hospital, where a respirator was made ready for immediate use when indicated. The temperature throughout had ranged between 98.6 and 100 F.; the pulse rate between 98 and 120; respiratory rate between 22 and 28.

The child was transferred at 12:30 p. m., and Dr. Dalton Phillips, resident in pediatrics at Grasslands Hospital, supplied the following progress notes: On admission all four extremities were flaccid and immovable; the gag reflex was absent but there was no respiratory paralysis. There were positive Kernig sign bilaterally and generalized hyperesthesia to pin prick. A respirator of the Emerson type was in immediate readiness, and the patient was given 500 cc. of isotonic sodium chloride solution by venoclysis. Nasal oxygen administration was started. Eight hours after admission, sensorium cleared and she moved all four extremities in bed.

Twenty-four hours later, all reflexes had returned except for absent biceps reflex and hypoactive left triceps and extremities were much stronger. Abdominal reflexes were still absent. Two days later there was complete recovery. She was kept under observation for three more days. Temperature was normal until the fourth day of hospitalization, when it rose to 101 F., which was attributed to the markedly positive Schick reaction on admission. She was discharged after five days in excellent condition.

Laboratory Findings.—July 25: Laboratory data were the following: hemoglobin 11.4 gm. per 100 cc.; red blood cells 3,500,000 per cubic millimeter; white blood cells 5,400 per cubic millimeter, with 51% lymphocytes, 3% eosinophiles, and 46% polymorphonuclear leucocytes (no myeloblasts, 2% nonsegmented forms, and 44% segmented forms). Urine analysis showed rare white blood cells and rare red blood cells. Blood sugar was 114 mg. per 100 cc., nonprotein nitrogen 28 mg. per 100 cc. Spinal fluid was clear, colorless; pressure, 140 mm.; there were no cells present. The Pandy test showed a slight trace of globulin; culture showed negative results. The sedimentation rate (Wintrobe method) was 15 mm. in one hour.

July 26 (Grasslands Hospital): The laboratory data were the following: hemoglobin 10.5 gm. per 100 cc.; red blood cells 3,110,000 per cubic millimeter; white blood cells 17,200 per

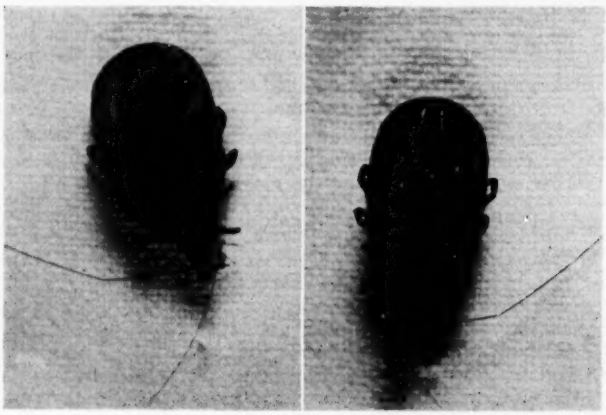

Fig. 3.—Engorged D. variabilis Say removed from patient; left, posterior view, showing mouth parts with epidermis; right, anterior view, showing detached epidermis (magnified approximately 10 times).

cubic millimeter, with 86% polymorphonuclear leucocytes and 14% lymphocytes. The urine showed no abnormalities. The spinal fluid showed one cell; the Pandy reaction was negative, the colloidal gold curve negative, total protein 18 mg. per 100 cc., chloride 740 mg. per 100 cc., sugar 64 mg. per 100 cc. The sedimentation rate was 28 mm. in one hour. Spinal fluid and blood Wassermann tests gave negative results. Throat culture showed growth of Hemophilus hemolyticus and Staphylococcus aureus. Roentgenograms of the skull and chest showed no abnormalities.

The removed tick was sent to the United States Public Health Service, at Bethesda, Md., and was identified by Dr. Paul A. Woke,[28] of the Laboratory of Tropical Diseases, as "an almost fully engorged female tick Dermacentor variabilis. Eggs were developing in this specimen, but since the tick was dead and preserved, we had no way of determining whether fertile eggs would have been procduced." Photographs of the tick removed are shown in Figure 3.

Follow-up of the patient to seven months after the onset of the paralysis (February, 1951) showed complete recovery without weakness of any muscle group.

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28. Woke, P. A. (Laboratory of Tropical Diseases, Microbiological Institute, National Institutes of Health, Bethesda, Md.): Personal communication to the author.

COMMENT

The above case showed the clinical and laboratory findings typical of this disease. It also demonstrated the rapidity of progressive signs from asthenia to bulbar paralysis, increasing for a few hours even after the removal of the tick, as well as the dramatic improvement following the removal.

Rarity of Tick Paralysis.—Since ticks are very common, why is the disease so rare? Ransmeier [2d] has presented some explanations. Before an attempt is made to offer further thoughts on this subject, certain other data which have been acquired from the literature and from personal communications will be set forth:

1. The ratio of adult female ticks to male ticks is about 1:1, with a slight preponderance of females.[29]

2. Whereas in New York State, Rocky Mountain spotted fever, prior to 1942, occurred in five to nine cases yearly, since then, 15 to 17 cases yearly are being reported, all originating on Long Island (exclusive of New York City).[30] Three cases of Rocky Mountain spotted fever have so far been reported in Westchester County, all originating in other localities.

3. The personal observations of six veterinarians contacted indicate that in the northern part of Westchester County ticks in dogs were rare up to 15 years ago, the few cases being imported from Long Island or Cape Cod. Now from 10 to 12 dogs are being deticked daily, although the increase has not been as marked in the past five years. These cases are seen mostly in the spring and early summer, with the peak during April and May, depending on the rainfall or humidity.

4. Heavy infestation is present in Cape Cod, where no cases of paralysis have been officially reported.[31]

5. One to two cases of tick paralysis in dogs are being seen yearly by Dr. Albert Pontick, D. V. M., in East Hampton, Long Island. He reports "partial to complete flaccid paralysis of not only the hind limbs but of the entire body in extreme cases. Simply removing the tick . . . effects a rapid uneventful recovery." [32]

6. In the life cycle of the tick, egg production normally follows the ingestion of a full blood meal. The tick normally detaches itself within one day of full engorgement. Ticks mate by copulation during the period of engorgement of the female. In the absence of mating, the female continues engorgement and infertile eggs may be laid. Egg laying, regardless of fertilization, commences within a few days of detachment.[28] Engorgement of the female takes from 5 to 13 days, during which time mating takes place. In from 3 to 58 days, depending upon the temperature, after the engorged female drops from the host, egg laying begins. An engorged female may lay from 3,000 to 6,500 eggs, after which she soon dies.[33]

With all the above in mind, it is difficult to visualize that the bite of any engorged female tick is enough to cause the disease. One would expect many more dogs to have paralysis, and more human beings to have the disease, since engorged ticks are frequently removed from dogs and children without any symptomatology except for local irritation. The question, therefore, arises: Are all female engorged ticks capable of producing paralysis in man or animal, or must the eggs be fertilized?

This question can be answered only by further observation. It is suggested that once this clinical picture is recognized, the tick be removed intact and alive and be

29. Bishopp and Trembley.[24] Smith, Cole, and Gouck.[25]

30. Health News, New York State Department of Health **22**:65 (April 23) 1945. Collins, D. L. (State Entomologist, New York): Personal communication to the author.

31. Feemster, R. F. (Director, Division of Communicable Diseases, Massachusetts Department of Health): Personal communication to the author.

32. Pontick, A.: Personal communication to the author.

33. Report of the Department of Public Health, Commonwealth of Massachusetts, Relative to the Eradication and Control of Wood Ticks, House Bull. **2154**:14 (Dec. 1) 1948.

sent to a laboratory equipped with the facilities for proper identification of the ticks and of the eggs. It will be able (1) to ascertain the state of fertilization and (2) to duplicate the experimental effect of egg emulsions on laboratory animals as done by Prince, Keeley, and Scott. It is also important to save all engorged ticks found on all human beings, for proper identification, and in order to evaluate accurately whether eggs are present or not and, if present, why that patient was unaffected.

It is possible that another factor is present besides the mere bite of a female tick, i. e., an individual susceptibility or affinity to the specific neurotropic toxin of the tick, which might be comparable with the causation of encephalitis in primary vaccinia of later childhood as suggested by Ford.[34]

The cycle of the tick, as summarized above, may lend another explanation for the apparent rarity of the disease. If the tick takes from 5 to 13 days for full engorgement, is it not possible that the host be unaffected (or show minimal signs as weakness of the legs which has not progressed), since (1) the source of toxin was removed by the natural detachment of the tick or (2) the continued source of the toxin was removed, since it is probable that the tick had been found before full engorgement and coincidental egg production and maturation had occurred?

Is it not also possible that some transient unexplained cases of ataxia may be due to undiscovered tick bites, since the tick had detached itself?

Is it not also probable that some cases of tick paralysis are being misdiagnosed as poliomyelitis cases, since the seasons of incidence of these two diseases overlap? It must be remembered that in the bulk of tick paralysis cases so far reported the patients had been sent to poliomyelitis centers as poliomyelitis patients.

Importance of Recognition.—It is suggested that since this disease may be easily overlooked and may prove fatal, local health departments in infested areas conduct timely campaigns to warn both physicians and the public of tick-borne diseases, and to recommend periodical inspection of children, particularly girls, twice a day for attached ticks. It has been estimated that it takes from four to eight hours for a tick to become attached. A deticking program would save a life some day. Many people who conscientiously detick a dog pay no attention to their children, since they are not aware that ticks can be harmful.

TREATMENT

Once the syndrome is recognized, treatment is very simple. The tick must be found and removed, and it must be remembered that more than one tick may be present. The following procedure may be followed:

A. *Finding of Tick.*—The tick may be attached anywhere on the body, especially in dark and hairy areas, such as scalp, axillae, pubis, eyebrows, and perineum. It must be remembered that the engorged tick, which measures about ⅜ by ½ in. (10 by 13 mm.), becomes grayish in color and oval in shape and may be easily mistaken by the inexperienced for a pedunculated fibroma or wart.

B. *Removal of Tick.*—Removal of the tick *in toto* with the mouth parts intact is essential, since in one case with death reported the death was attributed to the continued action of the toxin contained in the salivary glands of the mouth parts left in place.

Many different techniques have been advised, including use of volatile irritating substances, as a drop of ether, gasoline, kerosene, benzine, on the head of the tick in order to make it lose its

34. Ford, F. R.: Diseases of the Nervous System in Infancy, Childhood and Adolescence, ed. 2, Springfield, Ill., Charles C Thomas, Publisher, 1944, p. 602.

grip. Also, application of warm substances, as a lit cigarette or match, to the tick and burying of the entire tick under petrolatum have been suggested. When using any of these techniques, it is essential to wait a full 10 minutes before expecting the tick to loosen its grip, so that removal with forceps may be easy.

In removing with forceps, one must be cautious to apply a gentle, steady traction. Twisting or rotation may break the tick. With a steady, straight pull, the tick comes away entire, with a small area of epidermis attached to the mouth parts. If this fails, the method recommended by Parker [35] may be used: Raise the skin adjacent to the tick with sterile forceps, making a tent, and undermining this area with sterile needle or scalpel. As the tick is removed with forceps, the superficial layer of epidermis will be detached with the mouth parts intact.

C. *Supportive Treatment.*—Supportive treatment consists in the following measures: 1. Bulbar paralysis should be treated by administration of oxygen, preferably by the nasal route, until the effects of the toxin are worn off. 2. The respirator is to be used only in well-justified cases, since in some cases in which it was tried it interfered instead of helped. 3. Suction with postural drainage should be used to clear pharyngeal secretions. 4. Hydration by parenteral infusions should be used if swallowing difficulty has been of long standing.

SUMMARY

A case of tick paralysis is reported, the first from Westchester County. Since a marked increase in the tick population has been observed here in the past decade, it is important to recognize its existence.

This is the second case in New York State, the third reported north of the Mason-Dixon Line, the 21st reported east of the Mississippi.

A summary of cases reported in the Eastern United States since 1946 is included, with a review of the previous cases.

The patient presented a rapidly ascending paralysis of the Landry type, with cranial nerve involvement (loss of speech and deglutition), which refutes the theory that the bite of D. variabilis causes a less severe syndrome than that of D. andersoni. Tick paralysis must always be considered (in tick-infested localities) in patients presenting flaccid paralysis.

Recognition of the disease early is essential to save life. Its incidence during the summer months coincides with the poliomyelitis season; differential diagnosis is imperative, since removal of the tick produces dramatic improvement even when bulbar paralytic symptoms have appeared.

Several points are raised in an effort to explain the apparent rarity of the disease.

It is suggested that local health departments in tick-infested areas conduct a campaign of education of the public each spring.

It is also suggested that a more intensive study of all ticks found on all human beings be conducted, since upon analysis of reported cases and in experiments it appears that only fertilized eggs contain the toxin responsible for this disease.

Dr. Robert A. Fox, Pathologist at the Northern Westchester Hospital, photographed the tick, and Dr. Dalton Phillips, Pediatric Resident of Grasslands Hospital, supplied progress notes and additional laboratory data.

35. Parker, R. R.: Cited by Abbott.[11]

Abstracts from Current Literature

Biochemistry; Bacteriology and Pathology

THE MECHANISM OF ANTIBODY PRODUCTION. C. O. STALLYBRASS, Proc. Roy. Soc. Med. **43**:137 (March) 1950.

Recent advances in relation to the biochemistry of genes, viruses, bacteria, and the granular biosomes of cells point to the important functions performed by nucleoproteins. Early hypotheses of antibody-production mechanism are either known to be or probably are fallacious. What does appear likely is that the plasmagene (ribose nucleic acid) and the antigen enter into a symplex and effect production of a new plasmagene symplex or system and control the production of the new globulin. With this the intracellular enzymes and building blocks would be diverted largely to the building of the new globulin, but the production of normal globulin would be simultaneously stimulated, and a large increase of normal globulin might ensue. This hypothesis is not simple, but neither is the normal twofold specificity of animal antibodies. It is largely a modification of previous hypotheses, notably that of Burnet.

HEARD, Monterey, Calif.

CLINICAL SIGNIFICANCE OF COLD AGGLUTININS IN CHILDREN. JAROSLAV REJLEK, Pediat. listy **5**:252, 1950.

A total of 323 blood samples from 263 children between the ages of 1 and 12 years were examined for cold agglutinins. The agglutination was always tested against their own blood cells.

The titer of the cold agglutinins in noninflammatory diseases never surpassed 1:16. This titer is considered as the upper limit of normal. In acute infectious diseases a slightly increased titer of 1:32 or 1:64 was often found. On the whole the range of the height of the titers and their frequency did not differ from values found among adults by other authors.

FROM THE AUTHOR'S SUMMARY.

Metabolism; Infant Feeding; Milk and Other Foods

THE PREVENTION OF THE FLUID-ELECTROLYTE "PROBLEM" BY SIMPLE MEANS. RICHARDS P. LYON, California Med. **73**:303 (Oct.) 1950.

Proper fluid balance may be maintained in patients after operation by the employment of simple, inexpensive procedures which may be carried out even in the smallest hospitals.

Daily weighing of patients, measurement of fluid intake and output, and knowledge of the probable electrolyte content of fluid losses are adequate guides for replacement of fluids and electrolytes. An increase in body weight is a warning of overhydration.

The content of the solution used for replacement is dictated by the route of fluid output—whether from the gastrointestinal tract, the skin, or the kidneys. Insensible losses (by perspiration and respiration) are fairly static. Except to replace extrarenal losses, parenteral administration of isotonic sodium chloride solution in the immediate postoperative period is contraindicated.

PRYOR, Redwood City, Calif.

AMINO ACID COMPOSITION OF EGG PROTEIN. J. C. LEWIS, N. S. SNELL, D. J. HIRSCHMANN, and HEINZ FRAENKEL-CONRAT, J. Biol. Chem. **186**:23 (Sept.) 1950.

Amino acid analyses of a number of egg proteins were made, utilizing both microbiological and chemical assay methods. The results of these analyses are presented in detail.

FORBES, Dallas, Texas.

THE ESSENTIAL AMINO ACID (EXCEPT TRYPTOPHAN) CONTENT OF COLOSTRUM AND MILK OF THE COW AND EWE. K. A. KUIKEN and P. B. PEARSON, J. Nutrition **39**:167 (Oct. 10) 1949.

The amino acid patterns of the milk and colostrum of the cow and ewe are very similar. The colostrum and milk of the two species were assayed for arginine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, threonine and valine by microbiological methods. Milk protein from each of these animals contains about 1.4 times the amount of methionine found in the protein of colostrum but only about 0.6 as much threonine. In the case of the other amino acids the relative proportions are more nearly equal. Kuiken and Pearson's data relating to the essential amino acids in cow's milk are in general agreement with values previously reported.

FREDEEN, Kansas City, Mo.

THE NUTRITIVE VALUE OF CANNED FOODS: I. AMINO ACID CONTENT OF FISH AND MEAT PRODUCTS. MAX S. DUNN, MERRILL N. CAMIEN, SAMUEL EIDUSON, and RUTH B. MALIN, J. Nutrition **39**:177 (Oct. 10) 1949.

A joint study has been made by Dunn and co-workers and Elvehjem and Strong and collaborators at the University of Wisconsin, with the cooperation of the National Canners' Association and the Can Manufacturers' Institute, of the amino acid composition of fish and meat products and the findings are presented in this paper. The distribution of amino acids was generally uniform. It seems of particular significance that none of the 13 amino acids determined was present in significantly lower amounts in the canned products than in the corresponding raw samples of fish and meat products.

FREDEEN, Kansas City, Mo.

THE NUTRITIVE VALUE OF CANNED FOODS: II. AMINO ACID CONTENT OF FISH AND MEAT PRODUCTS. J. B. NEILANDS, R. J. SIRNY, I. SOHLJELL, F. M. STRONG and C. A. ELVEHJEM, J. Nutrition **39**:187 (Oct. 10) 1949.

The authors' data give evidence of the reliability of the microbiological assay technique for amino acid analysis. Heat processing as employed in canning did not change materially the essential amino acid composition of the various fish and meat samples assayed.

FREDEEN, Kansas City, Mo.

THE EFFECT OF HEAT TREATMENT ON THE NUTRITIVE VALUE OF MILK PROTEINS: I. EVAPORATED AND POWDERED MILKS. BESSIE B. COOK, AGNES FAY MORGAN, ELSIE O. WEAST, and JANICE PARKER, J. Nutrition **44**:51 (May) 1951.

Data are given which show that preheating of powdered skim milk at 63 C. for 30 minutes or at 88 C. for 15 minutes and sterilization of evaporated milks at 115 C. to 116 C. for 15 minutes caused a slight decrease in the protein efficiency of the proteins, when measured by the rat growth method.

FREDEEN, Kansas City, Mo.

THE EFFECT OF HEAT TREATMENT ON THE NUTRITIVE VALUE OF MILK PROTEINS: II. RAT GROWTH STUDIES WITH CASEIN AND LACTALBUMIN AND THEIR LACTOSE DERIVATIVES. BESSIE B. COOK, AGNES FAY MORGAN, BEATRICE SINGER, and JANICE PARKER, J. Nutrition **44**:63 (May) 1951.

A significant decrease in the protein efficiency of lactalbumin for the growth of rats was produced by heat only in samples which contained lactose or which had been chemically reacted with lactose. The growth values of both heated and unheated lactalbumin were slightly improved by supplementing them with the amino acids valine, leucine, threonine, methionine, and arginine; lysine improved only the unheated protein. Histidine depressed the growth value of both the unheated and the heated lactalbumin, and when combined with lysine it depressed the value of the unheated protein. Only ornithine lessened the difference in growth values caused by heat treatment of lactalbumin. The apparent depression in the protein efficiency of the casein refluxed with water and heated and that refluxed in a lactose solution when lysine was added is difficult to explain. Three forms of change in the nutritive value of the casein appeared

to be involved: that caused by water washing alone, apparently not involving lysine and not aggravated by heating; that caused by dry heat, and partially restored by lysine, and that caused by reaction with lactose under the mild conditions, and reparable by lysine. This last change was aggravated by additional heat, which caused decreased availability of the other amino acids, with the result that the damage was not corrected by lysine.

FREDEEN, Kansas City, Mo.

DIETARY CONSTITUENTS WHICH MAY INFLUENCE THE USE OF FOOD CHOLESTEROL: 1. EGGS; BIOTIN AND AVIDIN. RUTH OKEY, R. PENCHARZ, S. LEPKOSVKY, and ELEANOR R. VERNON, J. Nutrition **44**:83 (May) 1951.

It is impossible to make a diet high in cholesterol by giving whole egg without at the same time rendering it high in at least two substances, protein and choline, which are rated as potent lipotropic agents. The data indicated that biotin and avidin affect liver cholesterol storage when the basal diets are high in methionine-rich protein as well as in the choline-containing phospholipid. Esterification and storage of cholesterol in the liver are normal responses to ingestion of a cholesterol-rich diet by the rat, and responses apparently dependent upon the availability of biotin. When biotin is lacking, esterified cholesterol disappears from the liver, and there is a spectacular loss of subcutaneous and visceral fat. The comparative well-being of the otherwise adequately fed rat with a mild biotin deficiency together with his ability to ingest a cholesterol-rich diet without excess storage of liver cholesterol ester suggest that avidin may possibly be of use to help to clear out tissue cholesterol deposits. However, experimental data indicate that its use in this connection would be of doubtful value.

FREDEEN, Kansas City, Mo.

NUTRITIONAL IMPROVEMENT OF WHITE POLISHED RICE BY THE ADDITION OF LYSINE AND THREONINE. LOUIS J. PECORA and JAMES M. HUNDLY, J. Nutrition **44**:101 (May) 1951.

These results indicate that lysine and threonine are the most deficient essential amino acids in rice and that they are about equally limiting for rat growth.

FREDEEN, Kansas City, Mo.

NITROGEN REQUIREMENT OF NORMAL MEN ON A DIET OF PROTEIN HYDROLYSATE ENRICHED WITH THE LIMITING ESSENTIAL AMINO ACIDS. WILLLIAM S. HOFFMAN and GORDEON C. MCNEIL, J. Nutrition **44**:123 (May) 1951.

Nitrogen balance experiments were performed in seven male human subjects to determine the nitrogen requirements for equilibrium when the only significant source of nitrogen was a lyophilized modified casein hydrolysate given orally. Then in the same subjects the nitrogen requirement for equilibrium was determined for the same hydrolysate fortified with *dl*-tryptophane, *l*-phenylalanine, and *dl*-methionine in quantities that made the quantitative pattern of essential amino acids in the supplemented product equivalent to that found by Rose in his estimation of the minimum requirements of the individual amino acids in human subjects. The corrected mean nitrogen requirement for equilibrium wth the unsupplemented hydrolysate was 52.2 mg. per kilogram a day, and for the supplemented product, 38.5 mg. per kilogram a day.

FREDEEN, Kansas City, Mo.

GALACTOSEMIA. G. N. DONNELL and S. H. LANN, Pediatrics **7**:503 (April) 1951.

Four cases of galactosemia are presented. Three of these occurred in one family. Autopsy findings in one case revealed portal cirrhosis and fatty infiltration of the liver.

The clinical features common to all were failure to develop and gain weight normally, vomiting, jaundice, and hepatomegaly. Lenticular cataracts were present in two of the cases. Glycosuria and albuminuria were consistent laboratory findings in all. Carbohydrate studies on two of the patients revealed marked intolerance to galactose. Clinical improvement followed the removal of lactose from the diet.

The etiology of hepatomegaly and the genetic aspects of the disease are discussed. The importance of identifying the reducing substance in patients with glycosuria is emphasized by the cases reported here.

FROM THE AUTHORS' SUMMARY.

PROTEIN AND AMINO ACID REQUIREMENTS OF INFANTS. ANTHONY A. ALBANESE, Pediatrics **8**:455 (Oct.) 1951.

Evidence has been presented which supports the view that the nutritional inadequacy of unsupplemented breast feeding of infants beyond the third month of life arises primarily from quantitative rather than qualitative limitations of certain amino acids. On the basis of amino acid composition data and the biologic value of a number of proteins tested in infants, it appears that to overcome the defects of this feeding practice, which still prevails in large areas of the world, the necessary diet supplements should be derived principally from animal protein sources, milk and meat, rather than from cereal proteins. In the event of a lack of animal foods, soybean milk may be employed to advantage.

FROM THE AUTHOR'S SUMMARY.

MALIGNANT MALNUTRITION: PREVENTIVE ASPECTS. I. MIRVISH, South African M. J. **25**:472 (July 7) 1951.

The role of protein-deficient diets in the etiology of malignant malnutrition is demonstrated, and the possibility of prevention by use of cheap plant proteins is discussed. The syndrome is found in poorer economic groups, for whom the expense of animal proteins is too great to permit their adequate usage in the diet.

McGUIGAN, Evanston, Ill.

COMBINED EFFECT OF SPECIFIC DYNAMIC ACTIONS OF FAT, CARBOHYDRATE, AND PROTEIN. A. DEGLI ESPOSTI, Clin. pediat. **31**:385 (July) 1949.

Studies were done on 10 children, 7 to 12 years of age, as to the specific dynamic action following the ingestion of 24 gm. of sugar, 25 gm. of butter, and 25 gm. of meat singly and in combination. The mean increases in metabolism were as follows: sugar, 6.5%; butter, 6.4%; meat, 23.1%; sugar and meat, 13.6%; butter and meat, 10.3%; butter and sugar, 6.6%; butter, sugar, and meat, 9.3%. It is apparent that simultaneous ingestion of sugar and fat will lower the specific dynamic action of protein.

HIGGINS, Boston.

THE EFFECT OF THE OXYMETHYL AMIDE OF NICOTINIC ACID ON ARTIFICIALLY FED INFANTS WITH "COW'S MILK DYSPEPSIA" AS DESCRIBED BY MARFAN. A. DEGLI ESPOSTI, Clin. pediat. **31**:449 (Aug.) 1949.

Twenty bottle-fed infants with dyspepsia, apparently due to a lowered liver function, were given two daily doses of 0.25 gm. of bilamid (the oxymethyl amide of nicotinic acid) over a period of 15 days. The infants showed clinical improvement, with better digestion and absorption of their food. Control observations on five infants who were given nicotinamide did not show the same improvement.

HIGGINS, Boston.

THE METABOLISM OF KETONE BODIES IN CHILDREN. P. TOLENTINO and G. CAFFARÉNA, Minerva pediat. **1**:437 (Dec.) 1949.

A proprietary product, "antiketon," containing a pancreatic extract, vitamin B, and some glycolytic ferments, had little or no effect in lessening the ketonemia or the ketonuria of children on a ketogenic diet or of children who had received acetone intravenously.

HIGGINS, Boston.

THE INTRAVENOUS ADMINISTRATION OF ACETONE AND THE METABOLISM OF THE KETONE BODIES IN NORMAL AND PATHOLOGICAL CONDITIONS. P. TOLENTINO, G. COTELLESSA, and G. CAFFARÉNA, Minerva pediat. **2**:410 (Sept.) 1950.

In a study of six normal children, four children with recurrent vomiting, and nine children with liver dyscrasias, 0.5 cc. of acetone per kilogram of body weight in 10 to 20 cc. of isotonic

sodium chloride solution was injected intravenously four hours after the last meal. Determinations were made of the blood level and of the urinary and respiratory excretion of acetone at frequent intervals.

The ketonemia might persist for much over 12 hours and was not necessarily quantitatively related to the respiratory and urinary excretion. Beta-oxybutyric acid began to be found in the blood after some hours. The amount of acetone excretion was very high in the expired air but rather small in the urine (5% of the total). About 30 to 60% of the acetone was excreted; the remainder was metabolized in the body. In some children with liver disease the metabolism of the acetone was very high, because of a great avidity of the tissues for the ketone bodies and the failure of the liver cells to produce them. This finding was so inconsistent that it is of no practical value as a test for liver function.

HIGGINS, Boston.

FOOD DEFICIENCIES IN NEOPOLITAN CHILDREN AND YOUTHS IN THE POSTWAR PERIOD JUDGED FROM THE RECOMMENDED DIETARY ALLOWANCES OF THE FOOD AND NUTRITION BOARD OF THE UNITED STATES NATIONAL RESEARCH COUNCIL. P. DE CAPRIO, Pediat. **57**:633 (Sept.) 1949.

A study was made in Naples by the Italian Medical Nutrition Mission in 1945 on the diets of 600 children and youths as compared with the dietary needs recommended by the United States National Research Council.

The diets of 183 children with obvious clinical lesions referable to nutritional deficiency had been extremely poor in calories and in animal protein. The diets of 67 children in apparently good nutritional state were lacking in vitamins A, in calcium, and in ascorbic acid. The diets of 200 boys, 13 to 18 years of age, in poor health had been low in calories and in protein. The diets of 150 boys of the same age and in fair health were deficient in calories, protein, calcium, iron, and all the vitamins except thiamine and riboflavin.

HIGGINS, Boston.

THE CAPILLARY AND VENOUS BLOOD SUGAR CURVES OF CHILDREN AFTER GLUCOSE, INSULIN AND ADRENALINE. G. R. BURGIO, Pediatria **58**:655 (Sept.) 1950.

The blood sugar curves of normal and of diabetic children take a standard characteristic type when insulin, epinephrine, or one feeding of sugar has been given. When sugar has been given in two feedings, there is no characteristic curve. The curves have been found to be different for different children, and for the same child in different tests.

HIGGINS, Boston.

ELECTROPHORETIC SERUM PROTEIN STUDIES IN CHILDHOOD. KROPP, Monatsschr. Kinderheilk. **98**:159 (April) 1950.

By means of electrophoretic studies it was found that albumin content was the same in the umbilical cord blood and blood of infants as in the blood of older children. Alpha globulin was present in cord blood in the same amount as in the blood of older children, but for infants it was higher. Beta globulin of umbilical cord blood was lower than in the blood of older children. Gamma globulin was high in cord blood and decreased during childhood.

HARTENSTEIN, Madison, Wis.

CONTRIBUTIONS TO THE KNOWLEDGE OF IRON AND COPPER METABOLISM IN CHILDHOOD: I. IRON AND COPPER LEVELS IN NORMAL CHILDREN. W. BRENNER, Ztschr. Kinderh. **65**:727, 1948.

The serum iron and copper levels of 100 children from birth to 13 years were determined, and it was found that there were consistent variations by age. During the first four days of life, the iron content of the serum drops abruptly whereas the copper level remains the same. From the 5th to the 30th day of life iron values increase rapidly (copper was not determined) and run parallel with the increasing values for serum bilirubin, evidently a result of blood destruction. From the 2nd to the 18th month, the iron level is relatively low, the copper level is high. This physiological low serum iron content offers an explanation for the frequent occurrence of anemias due to prolonged infections in this age group. Infections characteristically cause a decrease in iron and an increase in copper levels. Such anemias (iron deficiencies) can hardly be expected

during the first three months of life. From 19 months up to 13 years the iron level increases but does not reach the level of the adult, whereas the copper level falls. The elevated copper level during childhood is interpreted as a function of increased cell metabolism during this period. No difference in iron levels between the sera of breast-fed and of cow's-milk-fed infants was found.

GLASER, Chicago.

A SCHEME OF ARTIFICIAL FEEDING. OTTO GREGOR, Pediat. listy **4**:241, 1949.

A scheme of artificial feeding based on the caloric value of food and on the caloric need is reported.

FROM THE AUTHOR'S SUMMARY.

GLYCOGENOSIS: A FAMILIAL MIXED FORM IN TWO SISTERS. J. HOREJSI, J. PISAROVICOVACIZKOVA and J. VANEK, Pediat. listy **5**:259, 1950.

The clinical and anatomical findings in two sisters with glycogenosis were identical and corresponded with the mixed form of glycogenosis chiefly involving the liver and the heart. The liver exhibited a cirrhotic structure. The two patients died from the leptomeningitis originating from a primary lesion of the lung; the miliary dissemination was most marked in the lungs and in the spleen.

FROM THE AUTHORS' SUMMARY.

DIETETIC TREATMENT OF OBESITY IN CHILDREN. L. HOSTOMSKA, M. STRAKOVA, J. BLUDSKY, and J. DEDIC, Pediat. listy **6**:204, 1951.

A reduced diet for children which is used in the children's clinic is described. Only 50 to 60% of the caloric need is covered by this diet. The reduction is at the expense of carbohydrates and fats, which are allowed at a weight proportion of 4:1 or 3:1. A sufficient amount is secured, as well as sufficient vitamins (A, B, and C). For practical purposes, a plan for such reduced diets for children from 6 to 15 years is added, and the experiences of the authors in hospital and outpatient treatment are described.

FROM THE AUTHORS' SUMMARY.

BREAST MILK BANKS IN RURAL DISTRICTS. GERT VON SYDOW, Svenska läk.-tidning. **45**:929 (May 14) 1948.

The author describes the organization of the breast milk bank in Gothenburg and discusses the general principles and value of collecting surplus breast milk.

WALLGREN, Stockholm, Sweden.

AMINO ACIDS IN THE BLOOD OF INFANTS AND CHILDREN. A. C. VAN DER LINDEN, Maandschr. kindergeneesk. **17**:231, 1949.

After a brief description of microbiological amino acid assay, the results of the analyses of 14 different amino acids in the globins of babies, small children, and adults are given.

Five babies, four children, and eight adults were investigated, and in a number of cases significant differences between groups were found.

The results were compared with the figures from the literature for the amino acid content of mother's milk and cow's milk. Speculative suggestions are given for the amino acid requirements of the premature baby, in which an iron-resistant anemia sometimes develops.

FROM THE AUTHOR'S SUMMARY.

Vitamins; Avitaminoses

TONSILLECTOMY IN THE ALLERGIC CHILD. BEN F. FEINGOLD, California Med. **71**:341 (Nov.) 1949.

Edema is the chief factor in enlargement of tonsils of children with allergic disease.

In the absence of infection, tonsillectomy and adenoidectomy are contraindicated for the allergic child, except when obstruction is present.

Infection produces one of two distinct patterns when it influences allergic states, the pattern depending upon the nature of the infectious disease. Chronic infection of the upper respiratory tract in the allergic child produces a pattern simulating that of acute respiratory infection. If, in the presence of infected tonsils and adenoids, management of the allergic state does not produce results, tonsillectomy and adenoidectomy are indicated. Management of the allergic disease must be continued postoperatively.

Whether infection is present or absent, allergic disease can be controlled only through competent management of it.

PRYOR, Redwood City, Calif.

THE MINIMUM RIBOFLAVIN REQUIREMENT OF THE INFANT. SELMA E. SNYDERMAN, KATHERINE C. KETRON, HELEN B. BURCH, OLIVER H. LOWRY, OTTO A. BESSEY, LOREN P. GUY, and L. EMMETT HOLT JR., J. Nutrition **39**:219 (Oct. 10) 1949.

The data reported by Snyderman and associates indicate that in infants weighing 5.9 to 9 kg. an intake of riboflavin of 0.4 to 0.5 mg. per day is compatible with freedom from symptoms of riboflavin deficiency, maintenance of urinary riboflavin excretion at the critical point (the "point of minimum excretion"), and maintenance of presumed normal levels of riboflavin in the blood serum, red cells, and white cells. These data do not permit one to state what the absolute minimum requirement is, even under well defined conditions. The data suggest that the measurement of red-cell riboflavin may be of service in assessing the riboflavin nutritional status. These values during depletion were lowered to less than half the probable normal value. The percentage change was greater than for the white cells, which are also more difficult to measure. The serum values for free riboflavin might be useful, except that in the deficient zone the absolute values are exceedingly low and therefore difficult to measure with any accuracy.

FREDEEN, Kansas City, Mo.

VITAMIN A AND BETA CAROTENE IN THE MILK OF WOMEN UNDER NORMAL CONDITIONS. G. CALZETTI and M. LATO, Clin. pediat. **31**:497 (Sept.) 1949.

The amounts of carotene and of vitamin A in mother's milk generally are in a definite ratio to each other. The amount of vitamin A in the milk is highest during the first week of lactation and gradually diminishes as lactation continues. This may be due to depletion of the vitamin in the liver. No definite relationship between the amounts of fat and of vitamin A in mother's milk could be established. The vitamin A content was less in the milk of multiparas than of primiparas.

HIGGINS, Boston.

ACTION OF VITAMIN C AND P_2 ON THE BLOOD VESSELS OF THE SKIN AND ON THE ABSORPTION TIME OF INDUCED EDEMA. P. NICOLAJ, Clin. pediat. **31**:512 (Sept.) 1949.

Both vitamin C and vitamin P_2 diminish the fragility of the small vessels of the skin of children. Vitamin P_2 was found to prolong the absorption time of induced edema (pomphus), while vitamin C reduced the absorption time. Hence it appears that the mechanism of action of these vitamins differ from each other.

HIGGINS, Boston.

CITRIC ACID AND RICKETS. E. HEINZ, E. MÜLLER, and E. ROMINGER, Ztschr. Kinderh. **65**:637, 1948.

There are three possible ways in which citric acid may act to prevent or cure rickets—by increasing intestinal absorption of calcium, by furthering calcium transport, and by increasing calcium utilization in the bone. The authors investigated the first possibility in detail and divided the action of citric acid into its effect as an acid and its effect as a constituent of a soluble complex calcium salt. The acid effect is identical with the effect of other weak acids but does not suffice to explain its antirachitic action completely. The formation of a complex salt, which depends upon the pH of the intestines and is optimal in neutral solution, plays an important role in the infant in whom the pH below the jejunum is 6 or above. It is, however, necessary to obtain an optimal ratio of citric acid to calcium, since in high calcium concentrations insoluble calcium citrates are produced. Such an optimal ratio can be obtained in breast

milk or in diluted cow's milk, but not in undiluted cow's milk in which the high calcium content would require too high a citric acid concentration to make the solution palatable. The improvement of intestinal absorption of calcium by vitamin D is identical with the action of citric acid properly employed, but the mechanism—whether it is also by formation of a complex salt or by another mechanism—has never been clarified.

GLASER, Chicago.

FATAL CASE OF VITAMIN D INTOXICATION. HUGO JELKE, Svenska läk.-tidning. **45**:1350 (July 9) 1948.

A woman, age 54, had been operated on for nontoxic goiter at 35 years of age. During the following 12 years she was well. Then she began to suffer from tonic cramps in her arms and legs and had bilateral cataracts, which were operated on. Two years later hypocalcemia was found, and for three years she was treated, with excellent results, with dihydrotachysterol. After this time she was given 250,000 units of vitamin D daily for 18 months instead of the dihydrotachysterol. Five months after the start of this treatment her condition began to deteriorate. There were nodules on the forearms (biopsy showed vascular lesions and necrosis of the surrounding tissues). She displayed dyspnea, edema in her legs, excessive thirst, and emaciation. At examination hypertension, myocardial lesion, hypercalcemia, and renal deficiency with azotemia and polyuria were found. She died with uremia. The postmortem examination showed serious renal lesions with sclerosis and disseminated calcifications of the interstitial small arteries.

WALLGREN, Stockholm, Sweden.

Hygiene; Growth and Nutrition; Public Health

SOCIAL ASPECTS OF PERSONALITY IN CHILD GUIDANCE CLINIC PRACTICE. ALMENA DAWLEY and FREDERICK H. ALLEN, Am. J. Psychiat. **106**:462 (Dec.) 1949.

Dawley and Allen discuss the concept of the child guidance clinic, its functions and the methods now employed in carrying out these functions. The importance of good social work is stressed as a means not only of evaluating the personality of the child and the difficulties which bring him to the clinic, but also of studying the total surroundings in which he lives and with which he is in conflict over his psychologic drives. Particular stress is laid on the parent-child relationship and its influence on the child's emotional development.

JAHR, Omaha.

ORGANIZATION OF SERVICES FOR THE COLLECTION AND PROCESSING OF MOTHER'S MILK AND OF FOODS FOR INFANTS IN MILAN. P. BRUSA, Lattante **22**:1 (Jan.) 1951.

A small unit has been established for the collection and drying of mother's milk at a central location in Milan. At this unit formulas and solid foods for infants are also prepared.

HIGGINS, Boston.

MORTALITY AT BIRTH AND THE MEANS FOR COMBATING IT. JULIO A. BAUZÁ and JOSÉ INFANTOZZI, Bol. Inst. internac. am. protec. infancia **25**:25 (March) 1951.

The authors make the following suggestions in connection with reduction of mortality among newborn infants: 1. There should be more widespread establishment of health centers and prenatal clinics, with a bonus to be given for regular attendance. 2. Legislation should be enacted to protect pregnant working mothers, married or single, during the last month of pregnancy and the six weeks following childbirth. 3. A central social and legal service should be organized and provided with sufficient funds to give effective protection. 4. The number of beds for childbirth in public maternity hospitals should be increased and in less important cities maternity homes where mothers could stay during the first months of breast feeding should be established. 5. More public and private agencies for the protection of pregnant mothers (such as mothers' lunchrooms and mothers' classes) are needed. 6. Improvement is needed in home maternal care and in the care of the newborn in maternity hospitals, and these should be under the direction of specialized pediatricians. 7. Mother's milk banks should be established to ensure that there will be enough for all newborn infants requiring it. 8. Compulsory reporting to the Central

Service for the Protection of Childhood within 24 hours after birth of every newborn infant weighing less than 2,500 gm. (5½ lb.) is needed. 9. Suitably equipped centers with specialized personnel for the inpatient, outpatient, and home care of premature infants are needed.

FROM THE AUTHORS' SUMMARY.

FETAL AND NEONATAL MORTALITY AND BIRTH WEIGHT OF CHILDREN BORN OF PREDIABETIC MOTHERS. OLGA IMERSLUND, Nord. med. **40**:1880 (Oct. 15) 1948.

One hundred seven diabetic women gave birth to 428 children during the years preceding the onset of recognized diabetes. The neonatal mortality rate, including stillbirths, was 3.95%. On the basis of 462 pregnancies among these 107 women, the spontaneous abortion rate was found to be 7.4%. In a control group of 386 children born to 103 nondiabetic women comparable in age to the diabetic patients, the neonatal mortality rate including stillbirths, was 5.2%. In a total of 426 pregnancies among these 103 nondiabetic women there were 8.3% abortions. The average weight at birth of 226 infants born three years previous to the diagnosis of diabetes in the mothers was 3.571 gm., as against 3.500 gm. in children born of normal mothers.

WALLGREN, Stockholm, Sweden.

PHYSICAL DEVELOPMENT IN INFANCY. ALFRED SUNDAL, Tidsskr. norske lægefor. **68**:43 (Feb. 1) 1948.

The author has examined 100 male and 100 female full-term infants from birth on with regular weekly measurements of height and weight, and he presents the weight in a curve with mean values and normal variations for each week of the first year of life. The mean values of the height are registered on the same curve. The height and the weight are tabulated as follows: at birth 51 cm., 3,500 gm. ± 400 gm.; at 3 months of age 60.5 cm., 5,850 gm. ± 600 gm.; at 6 months of age 67.5 cm., 7,650 gm. ± 850 gm.; at 9 months of age 72.5 cm., 9,150 gm. ± 950 gm., and at 12 months of age 76 cm., 10,300 gm. ± 1,000 gm.

WALLGREN, Stockholm, Sweden.

Prematurity and Congenital Deformities

INSTINCTS AND EMOTIONS IN AN ANENCEPHALIC MONSTER. J. M. NIELSEN and P. P. SEDGWICK, J. Nerv. & Ment. Dis. **110**:387 (Nov.) 1949.

An anencephalic monster first seen at the age of 6 days is described. The infant slept, awakened, sucked, expressed hunger, fear, and contentment. The grasp reflex was well developed. The weight on entrance was 5 lbs. 9 oz. (2,520 gm.). There was no cranial vault but the scalp was redundant, covered with hair and appeared to have been a larger mass which had collapsed. There was a large midfrontal meningocele which was torn slightly at birth.

The electroencephalogram was negative, as was the roentgenogram, except for the skull, which showed collapse of the cranial bones. The child lived 85 days and died of frontal epidural abscess. At necropsy: no cerebral mantle was visible; in fact nothing was recognizable above the mesencephalic level, not even the thalamus.

The authors postulate that the cerebral cortex merely provides a receptor and motor mechanism by which instincts and emotions are expanded but is not essential to infantile instincts and emotions.

JAHR, Omaha.

FEEDING OF PREMATURE INFANTS. SOL M. ABELSON, J. Pediat. **37**:711 (Nov.) 1950.

The 311 premature infants in this study were fed a formula of half evaporated milk and half water. For the most part, they gained weight well. The death rate for the entire group was 17%, but, as Abelson notes, premature death rates are related more to obstetric difficulties and maternal disease than to infant diet.

Spontaneous acidosis occurred in eight infants but was never a serious complication. It might have been prevented by adding 2 cc. of 6% solution of sodium citrate to each 100 cc. of formula mixture.

No cases of retrolental fibroplasia were seen in this series. Water-dispersible vitamins were given, but no vitamin E was added to the diet. The author suggests that perhaps the high fat diet helped to prevent this eye complication.

MACDONALD, Pittsburgh.

TWO CASES OF CONGENITAL MALFORMATION OF THE HAND. A. GHIO and A. AGNESE, Lattante **22**:37 (Jan.) 1951.

Case reports of two infants with congenital absence of the phalanges on one hand are presented. The etiology of the malformations is regarded as obscure. HIGGINS, Boston.

STATUS BONNEVIE-ULLRICH. M. SCARZELLA and E. GIOVANNINI, Minerva pediat. **1**:409 (Nov.) 1949.

The case of a boy of 5 years with the Bonnevie-Ullrich syndrome is reported. The signs noted were dwarfism, pterygium colli, cutis laxa of the neck and breast, hypoplasia of the pectoral muscles, depressed nasal tip, epicanthic folds, slanting eyes, hypoplasia of the mandible, and congenital malformation of the heart. HIGGINS, Boston.

TWO PERSONAL OBSERVATIONS OF HURLER'S POLYDYSTROPHY. P. DEMOULIN, Acta pædiat. belg. **2**:189, 1948-1949.

Demoulin reports two cases of lipochondrodystrophy (Hurler's disease); the patients were 2 and 5 years of age. The author gives an exact description of the symptoms: large head; open fontanel; bossing of the frontal bones; deformities of chest, vertebral column, and hand bones; opacity of the cornea; hepatomegaly and splenomegaly, and physical and mental retardation. Chemical and morphologic studies of blood and urine showed normal results. The tuberculin and serologic syphilis reactions were negative. There was no consanguinity, nor was there a similar case reported in either family.

The author states that etiology and pathogenesis are still completely mysterious but that hereditary factors seem to play a role according to the reports of the literature, which were reviewed in some detail. GLASER, Chicago.

PATHOLOGICAL ANATOMY AND CLINICAL ASPECTS OF SPINA BIFIDA. HANS MOSER, Wien. klin. Wchnschr. **63**:21 (Jan. 12) 1951.

The differential diagnosis of myelomeningocele, myelocystocele, and meningocele is summarized in a table. Spina bifida occulta and cephalocele are also discussed.

AMBERG, Rochester, Minn.

CONGENITAL HYPERTROPHY OF METATARSALS AND TOES. K. S. FAN, Chinese M. J. **67**:450 (Aug.) 1949.

Fan's patient showed marked hypertrophy of the second and third toes of the left foot with accompanying hypertrophy of the corresponding metatarsals. The first metatarsal and big toe were underdeveloped, and their function as the chief weight-bearing structures in the medial side of the forefoot had been assumed by the hypertrophied second metatarsal and toe.

MACDONALD, Pittsburgh.

LITHOPEDIAN: GENERAL DISCUSSION AND CASE REPORTS. DANIEL S. P. TIEN, Chinese M. J. **67**:451 (Aug.) 1949.

Lithopedian is defined by Tien as the calcified or mummified remains of a fetus carried in the uterus, its appendages, or the abdominal cavity sometimes long beyond the normal period of gestation.

The case reported here is that of a calcified, mummified 7-month fetus of an abdominal pregnancy, the result of a ruptured left tubal gestation. This lithopedian had been tolerated for 25 years by a Chinese woman 43 years old. Two subsequent pregnancies were carried to term with spontaneous delivery. This is the 248th lithopedian reported in the literature since the report of the first such case, in 1557. MACDONALD, Pittsburgh.

PROGNOSIS OF PREMATURE INFANTS IN A CHILDREN'S HOSPITAL AS COMPARED WITH THAT IN MATERNITY HOSPITALS. I. BOESEN, Nord. med. **37**:418 (Feb. 27) 1948.

The comparison permits the conclusion that every hospital of a certain standard is able to offer such care for the premature babies within the first 10 days of life that a minimum mortality rate is ensured. In the 252 premature infants treated at the pediatric department the death rate was 75% for those with less than 1,000 gm. of birth weight; 62% for those of 1,000 to 1,499 gm. birth weight; 29% for those with 1,500 to 1,999 gm. birth weight, and 24% for those with 2,000 to 2,499 gm. birth weight. The infants were admitted when they were less than 2 days old, and the mortality rate was reckoned within the first 10 days of life.

WALLGREN, Stockholm, Sweden.

Newborn

THE ANTERIOR TUBERCLE OF THE FIRST CERVICAL VERTEBRA AND THE HYOID BONE: THEIR OCCURRENCE IN NEWBORN INFANTS. ARTHUR C. TOMPSETT JR. and S. W. DONALDSON, Am. J. Roentgenol. **65**:582 (April) 1951.

Roentgenograms of the chest of 500 newborn infants were reviewed. The location and incidence of ossification of the anterior tubercle of the first cervical vertebra and the hyoid bone is described. The anterior tubercle of the first cervical vertebra is ossified in 20.6% and the hyoid bone in 75.2% of normal infants.

HODGSON, Rochester, Minn.

INTESTINAL OBSTRUCTION IN THE NEWBORN. DONALD M. GLOVER and FRANK M. BARRY, Ann. Surg. **130**:480 (Sept.) 1949.

Vomiting in the newborn infant is too common to cause concern, but when the vomitus contains bile and when the abdomen is distended on the first day of life, the diagnosis should be considered to be intestinal obstruction due to an anomaly until proved to the contrary.

Factors contributing to high mortality rate are (1) the high incidence of prematurity and cardiac anomalies, (2) delay in diagnosis and hence operation, and (3) inadequate or unphysiologic operative management. Surgical errors rank high as probable causes of failure.

The authors discuss operative management and technical considerations. They report 47 cases.

BANTIN, Omaha.

A STUDY OF INFLATION OF THE LUNGS OF THE NEWBORN: A PRELIMINARY REPORT. A. C. HILDING, California Med. **71**:332 (Nov.) 1949.

There seems to be no reasonable doubt that the lungs in a newborn infant expand progressively during the first few days of life. Some degree of atelectasis seems to be perfectly normal. This is indicated by a number of roentgenographic studies (including those here reported), by the reported findings of pathologists, by the fact that in experimental animals the lungs inflated very unevenly, and by the fact that aeration of only a portion of the lung is needed for complete oxygenation of the blood. The relation of atelectasis to neonatal death is not entirely clear and is probably not always the same. The infant may die from other causes before the lungs are fully expanded. Atelectasis may develop secondarily to other debilitating conditions. The frequent coincidence of prematurity and extensive atelectasis is impressive. It may be that the lungs are so incompletely formed that they cannot expand. On the other hand, atelectasis and massive collapse in the adult is a serious condition, and there seems to be no good reason to suppose that this cannot also occur in infants and be serious per se.

The air pressures found necessary to expand the lungs in rabbit fetuses were found to be about 10 times what adult humans use in quiet respiration and were of about the same magnitude as the pressures found necessary to expand the lungs of stillborn humans. An attempt to produce atelectasis in newborn rabbits by chilling was most inconclusive. Atelectasis did develop in 3 of 15 animals used in the experiment, but the relation to chilling was not at all clear.

PRYOR, Redwood City, Calif.

HEMATOLOGIC FEATURES WHICH MAY INFLUENCE RH IMMUNIZATIONS. S. P. LUCIA and MARJORIE L. HUNT, California Med. **73**:250 (Sept.) 1950.

The biologic features which may influence Rh sensitization in the mother and hemolytic disease in the newborn are conditioned by the hereditary immunologic pattern of the subjects, the antigenic characteristic of the blood group-specific substances, the character of the antibody responses, the inherent susceptibility to disease as a result of the immune mechanism, and the character and sequence of exposure to the antigenic substance. In respect to Rh-negative women, there appears to be a greater vulnerability to immunization among those of blood group A. In regard to the infant, the compatibility of the maternal-infant blood types and the part they play in the competition of antigens may influence the occurrence of hemolytic disease in the newborn.

PRYOR, Redwood City, Calif.

RESUSCITATION OF THE NEWBORN INFANT: USE OF THE POSITIVE PRESSURE OXYGEN-AIR LOCK. ALLAN BLOXSOM, J. Pediat. **37**:311 (Sept.) 1950.

Bloxsom has designed a positive pressure oxygen-air lock for the resuscitation of the anoxic newborn infant. Pressure in this instrument is cycled between 1 and 3 lb. (0.5 and 1.3 kg.) at one-minute intervals. This apparatus promotes bronchial drainage and a more uniform alveolar aeration. It increases skin absorption of oxygen and relieves and protects against atelectasis. It provides breathing exercises and improves muscle tone. It combats acute pulmonary edema. Premature infants are especially relieved by this type of oxygenation; some have been sustained in the lock for as long as 10 days.

MACDONALD, Pittsburgh.

ERYTHROBLASTOSIS FETALIS: VII. TREATMENT WITH EXCHANGE TRANSFUSION. LOUIS K. DIAMOND, FRED H. ALLEN JR., and WILLIAM O. THOMAS JR., New England J. Med. **244**:39 (Jan. 11) 1951.

Exchange transfusion is the treatment of choice for babies with erythroblastosis fetalis, since it has been shown that its use has brought about a decrease in mortality, along with a marked reduction in the incidence of kernicterus.

The technical details of a method of exchange transfusion through a single plastic tubing, inserted into the umbilical vein, are presented, as well as an outline for after-care.

The authors list the indications for exchange transfusion. These are the following: (1) if the baby (less than 24 hours of age) has clinically apparent erythroblastosis fetalis; (2) if the baby is Rh positive, as demonstrated by direct testing or a positive direct Coombs' reaction, and the mother's titer of Rh antibody was 1:16 or higher at some time during the pregnancy; (3) if the baby is Rh positive and there is an unfavorable past history, particularly kernicterus in a previous sibling, regardless of the titer level, and (4) if the Rh positive baby is immature.

This article should be consulted for the important details which amplify the above points.

WHEELOCK, Denver.

VITAMIN E LEVELS IN TERM AND PREMATURE NEWBORN INFANTS. WINFIELD T. MOYER, Pediatrics **6**:893 (Dec.) 1950.

This study was done to establish the blood level of vitamin E in the newborn infant and to compare the level in the term infant with that in the premature infant at birth and immediately after birth. It was found that the vitamin E level at birth in 64 infants averaged 0.23 mg. per 100 cc., with a standard deviation of 0.13 mg. per 100 cc., for both term and premature infants regardless of birth weight. In term infants the average vitamin E level after five days increased to 0.36 mg. per 100 cc., while in the premature infants no increase in level was noted for the first two months of life. The vitamin E level in the premature infants between 3 and 6 months of age had increased to 0.50 mg. per 100 cc. In 33 term infants the average vitamin E level obtained from the cord blood was equal to the average level obtained from blood drawn from the infant within 24 hours after delivery, but these values in any one case varied as much as 50 to 75%.

FROM THE AUTHOR'S SUMMARY.

SOME OBSERVATIONS ON FACIAL PARESIS IN THE NEWBORN INFANT: ETIOLOGY AND INCIDENCE. W. R. HEPNER JR., Pediatrics **8**:494 (Oct.) 1951.

Eight hundred seventy-five consecutive mature infants of cephalic presentation delivered vaginally were examined for the presence of facial weakness. The incidence of facial weakness was 6.4%. The incidence was the same whether the infants were delivered with or without the aid of forceps. Of 159 infants delivered without the aid of forceps, 10 had facial paresis, which was on the same side as that of the obstetric position of the occiput. Of the 716 which were delivered with the aid of forceps, 46 infants had facial weakness on the same side as that of the obstetric position of the occiput. The spines of the maternal ischium can be discredited as a causal factor by the presence of transient facial pareses in infants delivered after a test of labor by Caesarean section without forceps. Roentgenologic demonstration of the anatomic relationship of the maternal sacral prominence, and not forceps trauma, is probably responsible for the majority of facial pareses seen in newborn infants.

FROM THE AUTHOR'S SUMMARY.

DIPHTHERIA WITH FALSE MEMBRANES IN THE NEWBORN. P. GIRAUD, R. BERNARD, and V. PILOTTA, Pédiatrie **36**:395 (Sept.-Oct.) 1947.

Three cases of pharyngeal diphtheria are described because of the rarity of this condition and its high mortality rate (85%). The immunity of the newborn is variable, and the negative Schick reaction in 90% of infants may signify an absence of immunity (infantile type: favorable to nasal diphtheria) or total immunity (adult type: favorable to the carrier stage). The positive reaction corresponds to a relative immunity (favorable to pharyngeal diphtheria), which was the case in the infants described by the authors. The symptoms were few: coryza, false membrane over anterior pillars and soft palate, with glandular swellings without edema. Extention to the larynx, paralysis of the palate, bronchopneumonia, and circulatory collapse may complicate the picture. In contrast to nasal diphtheria, the prognosis is bad and vigorous treatment indicated: early administration of antiserum and penicillin, cardiac stimulants, cortical extract with high doses of vitamin C, and stimulation with strychnine.

GLASER, Chicago.

SPONTANEOUS HEMOTHORAX IN A NEWBORN INFANT. RODOLFO BURDACH and ALEJANDRO MANTEROLA, Rev. chilena pediat. **20**:534 (Dec.) 1949.

The case history of a newborn infant who suddenly presented the symptoms of acute anemia and severe collapse is reported. The physical examination localized the hemorrhage as in the left pleural cavity, and a chest tap confirmed the diagnosis. Immediate treatment was begun with vitamin K and stimulants, plus fresh blood transfusions, followed by drainage of the effusion. The infant recovered rapidly. The cause of this spontaneous hemothorax could not be established, but there were certain facts that inclined the authors to postulate an association with a hemorrhagic disease of the newborn.

The chest roentgenogram, taken soon after birth, showed air-fluid lung shadows that owing to their characteristics and course were later interpreted as corresponding to those of a bullous emphysema of obscure mechanism.

FROM THE AUTHORS' SUMMARY.

COAGULATION OF THE BLOOD IN THE NEWBORN. HERNAN GARCES S., Rev. chilena pediat. **21**:191 (May) 1950.

In studying the blood-clotting mechanism in 24- to 48-hour old newborn infants, the author found that in the great majority of his patients there were clotting abnormalities, with values that are 50% lower than those found in normal adults. These derangements are found in children who are clinically normal as well as in those with hemorrhages.

The intensity of this blood defect is not in direct relation to the production of hemorrhages, but the strictly spontaneous hemorrhages do coincide with severe blood defects.

It is possible to improve and even to obtain "in vitro" normal values in a great number of these defective plasmas by the use of thromboplastic activators. In some cases there is particularly a fibrinogen defect, the other clotting factors remaining more or less active. In a severe case the absence of fibrinogen is concomitant with an absence of thrombin formation.

In the newborn there apparently exists, to great or small degree, a failure of the globulin complexes (beta and gamma globulin) that affects the clotting factors individually or *in toto*, a derangement that could be attributed to a relative liver insufficiency proper to this age period.

FROM THE AUTHOR'S SUMMARY.

RETINAL HEMORRHAGES IN THE NEWBORN. MIGUEL MILLAN A. and SERGIO BELTRAN SAN MARTIN, Rev. chilena pediat. **21**:209 (May) 1950.

Retinal hemorrhages in the newborn are common; in the authors' series they were found in 19.35% of the cases. Retinal hemorrhages are of venous origin, and the most important etiologic agents are, first, anoxia and, second, obstetrical trauma. There is no type of delivery that will guarantee absence of retinal hemorrhage.

These hemorrhages disappear with extraordinary rapidity. Apparently they do not leave sequelae, and the authors had not found any ophthalmological abnormalities during their one-year follow-up study, even in the severest cases.

The retinal hemorrhage in the newborn is not an index of brain hemorrhages. The authors are of the opinion that these hemorrhages do not form part of the hemolytic disease of the newborn, because they have not found a relation between these and other hemorrhages in the newborn period.

FROM THE AUTHORS' SUMMARY.

RH SHOCK IN THE NEWBORN. ERICH HUTH, Ztschr. Kinderh. **65**:431, 1948.

The author reviews the pathogenesis of erythroblastosis by a thorough study of the world literature (153 references) and considers the mechanism to be an anaphylactic Rh shock with the production of histamine or histamine-like substances, plus constitutional factors in the child. The therapeutic recommendations include nonspecific desensitization of the mother during pregnancy, blood transfusions, exsanguination transfusions of the newborn if needed, injection of plasma of healthy pregnant women with histamine-inhibiting amino acids (arginine, histidine, cysteine) or antihistaminic drugs, and oral and parenteral administration of amino acid mixtures.

GLASER, Chicago.

CONTRIBUTION TO RH TEST SERUM PRODUCTION. C. MOELLER and L. RUNGE, Ztschr. Kinderh. **66**:1, 1948.

In order to obtain a test serum for serial determinations, the authors gave several injections of Rh-positive blood to an Rh-negative mother who had given birth to an erythroblastotic child (fifth birth). They obtained a blood with high antibody titer which was well suited to be used as a test serum.

GLASER, Chicago.

MICROSEDIMENTATION IN THE NEWBORN PERIOD. R. GOSTOF and V. MYDLIL, Pediat. listy **5**:171, 1950.

Attention is directed to the micromethod for the estimation of the sedimentation rate, often omitted in pediatric microdeterminations; the relation of the micromethod to the macromethod is presented graphically. No relation of sedimentation rate to the birth weight of the newborn infant could be ascertained. Sedimentation rate was found to be independent of the existence of physiologic icterus. Factors influencing the rate of sedimentation, especially in the newborn period, are mentioned.

FROM THE AUTHORS' SUMMARY.

EPIDEMIC DIARRHEA IN THE NEWBORN. J. DVORAK, B. KOTT, and J. VACLAVEK, Pediat. listy **6**:213, 1951.

The etiology, clinical features, prophylaxis, and treatment of epidemic diarrhea in the newborn are described. A short statistical note on the epidemics in the hospitals of Most and Chomutov is given.

FROM THE AUTHORS' SUMMARY.

INFLUENCE OF THE PLACENTA IN HEMOLYTIC DISEASE OF THE NEWBORN. J. H. VAN BOLHUIS, Maandschr. kindergeneesk. **17**:99, 1949.

In the study 186 placentas were serologically investigated for the presence of Rh antigens. A suspension was made of the thoroughly washed placenta, and then the inhibiting effect on Rh antibodies was determined. There were 28 placentas of Rh-negative children, 36 of Rh-positive children suffering from hemolytic disease of the newborn, and 122 of healthy Rh-positive children. None of the placentas of the Rh-negative children adsorbed the Rh antibodies; 31 of the 36 placentas of the erythroblastotic children showed adsorption, and 16 of the 122 placentas of the healthy Rh-positive children showed adsorption too. From these results it was concluded that Rh antigens are present in only a small percentage of the placentas of Rh-positive children and that the antigen from the placenta, when entering the maternal circulation, is probably the cause of the immunization of the pregnant woman. The fact that in a family sometimes a healthy Rh-positive baby is born after there had been born erythroblastotic children, even when the father is homozygous Rh positive, can be explained by the finding that for not all Rh-positive children were there Rh antigens in the placenta.

VAN CREVELD, Amsterdam, Netherlands.

TETANUS NEONATORUM. J. H. DE HAAS, Maandschr. kindergeneesk. **17**:163, 1949.

After a brief review of the current literature on this subject, two cases of tetanus neonatorum are described. In both cases the origin of the infection happened to be the umbilical scissors. The incubation period was seven days for the successfully treated patient and four days for the patient who died.

In the treatment sedatives are of utmost value; a high dose of phenobarbital is recommended, also penicillin in a high dose (this also prevents complications), both to be administered orally to prevent convulsions which are stimulated by repeated injections. Serum is nowadays less important than it was before. Wound excision is practiced no longer.

The complication of spondylolisthesis is mentioned. The second lumbar segment was displaced posteriorly. Afterwards it returned spontaneously.

Recent literature suggests an increase of tetanus neonatorum in the Netherlands.

VAN CREVELD, Amsterdam, Netherlands.

Acute Contagious Diseases

POLIOMYELITIS. JOE R. BROWN and A. B. BAKER, J. Nerv. & Ment. Dis. **109**:54 (Jan.) 1949.

Fifty-nine cases of bulbar poliomyelitis are reviewed. The patients were all adults treated in the University of Minnesota Hospital in 1948. Twenty-six (46%) of the patients died, most of them from involvement of the respiratory or circulatory centers in the medulla or from added failure of the peripheral mechanism of the respiratory tract with resulting anoxia. Hemorrhagic pulmonary edema was the most prominent finding at necropsy. One patient without bulbar involvement died from massive pulmonary embolism.

As a result of their study the authors suggest the following four syndromes of bulbar poliomyelitis: (*a*) The group involving cranial nerve nuclei, with lesions chiefly in the motor nuclei of the cranial nerves; (*b*) the respiratory center group, with the predominant lesions in the ventral reticular substance of the medulla; (*c*) the circulatory center group, with the predominant lesions in the dorsal reticular substance; (*d*) the encephalitic group, with more diffuse lesions.

As a guide to treatment of bulbar poliomyelitis the authors suggest elective tracheotomy, adequate suction, and oxygen mixtures up to 40% under positive pressure, if pulmonary edema is expected; adequate humidification of the gas mixture; careful checking of the oxygenation by means of arterial oxygen determination and the use of the oxymeter; frequent moving of the patient to avoid hypostasis and thrombophlebitis; maintenance of nutrition by nasal feeding; prophylactic use of penicillin; avoidance of sedatives and stimulants; early closure of tracheotomy opening, and constant and intelligent nursing care.

JAHR, Omaha.

POSTVACCINAL ENCEPHALITIS IN INFANCY. H. J. LAWLER, J. Pediat. **37**:709 (Nov.) 1950.

Contrary to published opinions, postvaccinal encephalitis does occur in infants, and the mortality is impressively high. Lawler reports two cases. One patient, 5½ months of age, died; the other, 7 months of age, recovered.

MACDONALD, Pittsburgh.

HYPERTENSION IN POLIOMYELITIS WITH RESPIRATORY PARALYSIS. L. W. SENNETT, M. A. PERLSTEIN, M. B. ANDELMAN, H. E. BARNETT, and H. JOSEPHY, Pediatrics **7**:529 (April) 1951.

A case of sustained hypertension complicating acute protracted poliomyelitis with respiratory involvement is presented. Data of studies of the autonomic nervous system and the kidneys are given. Complete necropsy findings, including detailed examination of the central nervous system, are presented. The role played by the nervous system and kidney is discussed, and it is suggested that in this case the hypertension probably was due to neurogenic factors.

FROM THE AUTHORS' SUMMARY.

A SEVENTEENTH CENTURY CASE OF POLIOMYELITIS. WILLIAM J. MALONEY, Edinburgh M. J. **56**:304 (July) 1949.

The event occurred near Strasbourg in 1699. A boy of 6 was seized with weakness of both legs. The left leg recovered; the right leg did not, but remained lame for the remainder of the boy's life. The patient died of fever at the age of 40, and the affected leg was dissected by Jean Godfroy Salzmann, who later reported his findings. The disease was not recognized as such by Salzmann, but it is now reanalyzed by Maloney, who offers evidence that it was poliomyelitis, the earliest case on the record thus far.

MACDONALD, Pittsburgh.

MUMPS MENINGO-ENCEPHALITIS. S. J. R. MACOUN, Great Ormond Street J. **1**:37 (June) 1951.

A case of mumps meningoencephalitis is presented, with clinical and laboratory findings. No clinical evidence of mumps was present at any time. Diagnosis was established by serological tests.

MCGUIGAN, Evanston, Ill.

DOES SCARLET FEVER EXIST IN THE TROPICS? EUGENE STRANSKY and NATALIA S. FELIX, Ann. Pediat. **177**:15 (July) 1951.

The Dick test has been performed on a restricted number of persons of all ages in a tropical country, the Philippines. It has been found that the percentage of positive reactors is very low for infants, while for preschool children it is almost as high as in the temperate climate. For the school age there are almost no, for adults definitely no, positive reactions. As scarlet fever as a clinical entity is not observed in the tropics, scarlet fever is in the Philippines without any exception a subclinical infection.

The authors examined on a larger scale susceptibility to diphtheria with the Schick test. The results were published in the Philippines. Diphtheria is relatively frequent in the tropics, although less frequent and more benign than in the temperate climate. The percentages of positive reactors among the different age groups are almost analogous to those for the temperate climate.

FROM THE AUTHORS' SUMMARY.

INFECTIOUS HOSPITALS FOR ACUTE ANTERIOR POLIOMYELITIS. N. CARRARA, Lattante **18**:534 (Sept.) 1947.

Carrara advocates the sending of all patients with acute poliomyelitis to specific hospitals for that disease. He fears the danger of the spread of the disease by healthy carriers from one part of a general hospital to another.

HIGGINS, Boston.

ORAL ADMINISTRATION OF LIVING CULTURES OF STREPTOMYCES GRISEUS AS CURE OF PERTUSSIS AND ANEMIA. V. SAGGESE, Minerva Pediat. **1**:388 (Nov.) 1949.

Excellent clinical results have been obtained by the feeding of living cultures of Streptomyces griseus to patients with whooping cough. Certain types of anemia were also benefited by the same treatment; this is explained by the finding that the cultures contain antianemic vitamins.

HIGGINS, Boston.

SUSCEPTIBILITY TO SCARLET FEVER, NUTRITION, AND CONSTITUTION. FRITZ KUESTER and JOHANNES TRAUTSCH, Arch. Kinderh. **138**:65 (Jan.) 1950.

Basing their conclusions on the observation of 3,000 children with scarlet fever, the authors state that children who contract scarlet fever are heavier and greater in height than normal control children. In children observed during the prewar period greater weight corresponded with increased height. During the last years of the war and the postwar period the surplus in weight was greater than the increase in height among children examined. This leads the authors to the conclusion that in the second group the water content of the body tissues was increased.

The greater susceptibility to scarlet fever in the heavier and taller children is explained by the assumption that these children are suddenly overflooded with Dick toxin to a higher degree than normal children.

ARON, Chicago.

SIGNIFICANCE OF DAMAGING ENVIRONMENTAL INFLUENCES UPON THE COURSE OF DIPHTHERIA IN CHILDHOOD. K. ROGGE, Ztschr. Kinderh. **66**:6, 1948.

The author compares the course (not the incidence) of diphtheria in the native population with the course of the disease in refugee children (Lübeck's Children's Clinic). He found that the course leading to severe (spreading) and malignant form of the disease was not more frequent in the refugee population than in the indigenous population, and he comes to the conclusion that environmental factors have no influence upon the severity of the disease.

GLASER, Chicago.

RECURRENCE OF INFANTILE PARALYSIS. M. MEUNIER, Acta. pædiat. belg. **2**:89, 1948-1949.

The author had the opportunity of observing personally two attacks of infantile paralysis in the same person at an interval of 13 years. The first attack occurred at the age of 9½ months, the second at 14 years of age. Both attacks were accompanied by paralysis, but complete recovery ensued after the first illness, whereas the second attack left the child with a paralysis of the right shoulder and arm.

The author emphasizes that although recurrences of poliomyelitis are rare, they nevertheless do occur. It seems that for some patients, immunity does not develop and neutralizing substances are not shown in their blood. Clinical observations and experimental studies on monkeys point toward the possible existence of various causative organisms, related to each other but not identical. This hypothesis also offers an explanation for the variations in symptomatology and severity of the disease.

GLASER, Chicago.

COMPARATIVE STUDIES ON THE EFFECT IN SCARLET FEVER OF SODIUM PENICILLIN AND PROCAINE PENICILLIN IN AQUEOUS SUSPENSION. T. JERSILD and S. MEHLSEN, Acta. pædiat. **40**:118 (March) 1951.

In a comparison of two uniform scarlet fever groups treated over the same period with either penicillin sodium, two injections daily for six days, or penicillin procaine in aqueous suspension, one injection daily for six days (same daily dose), no definite difference was found in the therapeutic effect, as judged from the frequency of complications, duration of the primary rise in temperature, bacteriological findings, sedimentation rate, and antistreptolysin titers.

No local or general untoward effects from the treatment with penicillin procaine in aqueous suspension were observed.

FROM THE AUTHORS' SUMMARY.

HIGH ALTITUDE FLYING AND LOW PRESSURE CHAMBER IN THE TREATMENT OF WHOOPING COUGH. EINAR V. V. BERGQUIST, Nord. med. **39**:1459 (Aug. 6) 1948.

Bergquist reports carefully controlled studies on infants and small children suffering from pertussis. Twenty children were treated with flight (in two cases twice) at a level of 3,500 meters for 45 minutes, and 25 other children were treated with placement in a low-pressure chamber for 45 minutes. No influence on the cough through these measures could be demonstrated.

WALLGREN, Stockholm, Sweden.

TREATMENT OF WHOOPING COUGH WITH HIGH FLYING AND LOW PRESSURE. HARALD HARPÖTH, Nord. med. **41**:164 (Jan. 28) 1949.

Low pressure treatment for 90 minutes (pressure corresponding to flying at 3,500 meters) in 51 patients with whooping cough produced no difference in the attacks of cough, in comparison with a control group of 70 patients (25 per cent of the children in both groups showed improvement). The flight experiment was carried out with 101 children. The flight took place at 3,500 meters' altitude and lasted for 90 minutes. There was no control group. The flights resulted in an exacerbation lasting a day or two, followed in 60% of the cases by an improvement in the number, strength, and character of the attacks, also by increased appetite and sound sleep. These two groups of children were treated at home, and the intensity of the disease was judged from information given by the family.

WALLGREN, Stockholm, Sweden.

ACUTE PARALYTIC ANTERIOR POLIOMYELITIS AND LYMPHOCYTIC MENINGITIS. KNUD BRÖCHNER-MORTENSEN and FLEMMING RAASCHOU, Ugesk. læger **110**:1263 (Nov. 4) 1948.

The authors report on 77 patients with typical paralytic poliomyelitis and 294 patients with apparently primary lymphocytic meningitis treated at two hospitals in Copenhagen in the fall of 1947. The maximal prevalence of paralytic poliomyelitis was in October, whereas the highest incidence of lymphocytic meningitis was in August. The authors discuss the problem of identical etiology of these two diseases.

WALLGREN, Stockholm, Sweden.

Acute Infectious Diseases

TREATMENT OF ASCARIASIS IN CHILDREN: USE OF 1-DIETHYLCARBAMYL-4-METHYL PIPERAZINE DIHYDROGEN CITRATE (HETRAZAN®). JAMES N. ETTELDORF and LLOYD V. CRAWFORD, J. A. M. A. **143**:797 (July 1) 1950.

Fifteen patients infected with Ascaris lumbricoides were treated with 1-diethylcarbamyl-4-methyl piperazine dihydrogen citrate (hetrazan®). Of these, 11 were given 6 mg. per kilogram of body weight three times daily for 7 to 9 days, and only one continued to have ova in the stools. Five were given 3 to 5 mg. for three to eight days, and the stools of three of these continued to reveal the presence of ova throughout the course of treatment and the following month. Only two showed any evidence of toxicity. Three normal children were given as much as 10 mg. per kilogram of body weight three times a day for one week without evidence of toxicity. This treatment does not require fasting, purges, or enemas.

KIMBALL, Evanston, Ill.

RESPONSE OF THE SERUM HYALURONIDASE INHIBITOR AND MUCOPROTEIN TO ADRENOCORTICOTROPIC HORMONE IN RHEUMATIC STATES: MUCOLYTIC ENZYME SYSTEMS XV. F. H. ADAMS, V. C. KELLEY, P. F. DWAN, and D. GLICK, Pediatrics **7**:472 (April) 1951.

Corticotropin (ACTH) was administered to 13 patients with acute rheumatic fever and to two with rheumatoid arthritis. The following observations were made:

1. The elevated nonspecific hyaluronidase inhibitor concentration of the serum dropped rapidly, usually to normal values, within 10 to 15 days, and subsequently the values became subnormal. This seemed to follow closely the subjective improvement in the patient's condition.

2. The elevated serum mucoprotein concentrations slowly returned to normal over a period of three to four months.

3. In instances in which the corticotropin was withdrawn or the dosage was reduced before a substantial drop of the mucoprotein level had taken place, the disease recurred.

4. Corticotropin administered to a patient with combined diabetes mellitus and rheumatic fever effected an increase in the insulin requirement to approximately double that of the precorticotropin period. As the corticotropin was gradually withdrawn, the insulin need returned to the precorticotropin amount. The effect of corticotropin on this patient's rheumatic fever was similar to that of the others receiving the hormone. FROM THE AUTHORS' SUMMARY.

AEROBACTER INFECTIONS ON INFANT'S WARDS. MARGARET H. D. SMITH, C. G. LOOSLI, and M. H. RITTER, Pediatrics **7**:550 (April) 1951.

In the course of a study on the control of air-borne infection by means of triethylene glycol vapor, there occurred an outbreak of infection due to a previously undescribed encapsulated, Gram-negative rod.

The morphologic and cultural characteristics of this organism place it in the Aerobacter-Klebsiella group. It was readily identified by its ability to show capsular swelling in the presence of sera against types 23 and 32 Pneumococcus. Serologic studies showed it to be antigenically related to certain other strains of encapsulated, Gram-negative rods, but not to Friedländer's bacillus, Hemophilus influenzae, Meningococcus, or Pneumococcus other than the types mentioned above.

In some of the patients who acquired the organism mild respiratory infections or diarrhea developed, accompanied by fever, but most remained asymptomatic.

The organism spread in epidemic fashion in both wards receiving glycol vapor and control wards and was recovered from the nasopharynx of 50 patients of a total of 361 included in the study, also from numerous nurses, attendants, and visitors. In the course of the epidemic the ward environment (air, dust, furniture, bedclothes) became heavily contaminated. It is postulated that patients with profuse nasal discharge and diarrhea may have served to infect the ward environment, which in turn served as the source of infection to other patients.

FROM THE AUTHORS' SUMMARY.

HYPERVENTILATION-TOXICOSIS IN INFANT'S GRIPPE. E. KERPEL-FRONIUS, F. VARGA, K. KUN, and J. VONOCZKY, Ann. pædiat. **177**:1 (July) 1951.

Toxicosis with hyperventilation following infection presents a clinical picture characterized by coma, hyperventilation, and acetonemia in which diarrhea and vomiting are of less importance.

The blood circulation time is hardly prolonged; dehydration—without salt depletion—appears to be only secondary owing to increased water loss in the lungs. In the blood the significant findings are the reduction of the arteriovenous (sinus blood) oxygen and carbon dioxide differences, the high degree of acapnia, the hyperchloremia, the acetonemia, and the slight degree of blood concentration.

FROM THE AUTHORS' SUMMARY.

CERVICOSCIATIC RHEUMATISM (NOBECOURT'S SYNDROME). P. PALA, Ann. ital. pediat. **2**:509 (Dec.) 1949.

The author reports a case which because of its symptomatology and clinical course is included in the syndrome of cervicosciatic rheumatism of Nobecourt. The author notes that even in this case it is impossible to perceive the mechanism and connection of this rare painful association.

FROM THE AUTHOR'S SUMMARY.

ANTI-INFLUENZAL VACCINATION OF CHILDREN. E. SCHWARTZ-TIENE and S. VIRIDIS, Minerva pediat. **1**:381 (Nov.) 1949.

A group of 35 children were given a mixed anti-influenza (strains A and B) vaccine; 15 and 30 days later studies of the existing antibodies, proteinemia, white blood cell counts, and sedimentation rates of the children were made.

HIGGINS, Boston.

TREATMENT OF TYPHOID IN CHILDREN WITH CHLOROMYCETIN ADMINISTERED EVERY 12 HOURS. JULIO MENEGHELLO, OSCAR UNDERRAGA, and SANTIAGO RUBIO, Rev. chilena pediat. **22:25** (Jan.) 1951.

The authors report 44 cases of typhoid in which treatment was with chloramphenicol (chloromycetin®). The amounts given were 50 mg. per kilogram of body weight as the initial dose, followed by a maintenance dose of 25 mg. per kilogram every 12 hours until the temperature reached normal levels. After this period the dose was reduced to half, and therapy was continued for 14 days. Good recovery was observed in the 44 cases, and only two relapses are reported.

FROM THE AUTHORS' SUMMARY.

EPISTAXIS AS AN ACCESSORY SYMPTOM IN RHEUMATIC FEVER. J. L. KEYZER. Maandschr. kindergeneesk. **17**:254, 1949.

Five cases of rheumatic fever accompanied by severe epistaxis are presented. Often a fresh exacerbation starts with bleeding from the nose. Epistaxis has to be considered as an accessory symptom of rheumatic fever.

FROM THE AUTHOR'S SUMMARY.

CONGENITAL MALARIA. T. HALBERTSMA, Maandschr. kindergeneesk. **19**:263 (Oct.) 1951.

Halbertsma describes three cases of congenital malaria in which parasites in the child's blood were found on the 45th, 31st, and 10th days respectively after delivery.

FROM THE AUTHOR'S SUMMARY.

Chronic Infectious Diseases

EFFECT OF ANTIHISTAMINE MEDICATION ON THE TUBERCULIN REACTION IN CHILDREN. ELI FRIEDMAN and IRVING SILVERMAN, Am. Rev. Tuberc. **60**:354 (Sept.) 1949.

The effectiveness of antihistamine agents in practically or completely inhibiting histamine wheals, allergic wheals, and passive transfer wheals has been reported in several recent investigations. The results of the use of these agents on the tuberculin skin reaction in animals has led to conflicting reports. In this study children with positive tuberculin skin reactions were given oral doses of 60 mg. of tripelennamine (pyribenzamine®) daily. No inhibiting effects were noted. Oral doses of 240 mg. daily for four days were without effect on the tuberculin reaction in 10 children. It is concluded that in routine tuberculin testing the possible effects of antihistamine medication may be disregarded.

EUGENE SMITH, Ogden, Utah.

SOME PROBLEMS IN THE DIAGNOSIS OF MENINGEAL TUBERCULOSIS. W. M. JAMIESON, Edinburgh M. J. **56**:221(June) 1949.

Thecal puncture should be performed on the child who, along with evidence of primary tuberculosis, becomes feverish, listless, and "sick." Sometimes a benign serous reaction may alter the spinal fluid in these patients temporarily, and complete recovery may occur without treatment. Jamieson thinks that treatment may be safely withheld from these patients for a day or two of observation. However, increasing drowsiness and reduction of the sugar content of the spinal fluid are danger signs, and streptomycin administration should be started at once.

MACDONALD, Pittsburgh.

PARA-AMINOSALICYLIC ACID IN PULMONARY TUBERCULOSIS. NORMAN W. HORNE, Edinburgh M. J. **56**:239 (June) 1949.

Horne treated 13 tuberculous patients with paraaminosalicylic acid. Although there was striking improvement in isolated cases, the drug did not cure the tuberculosis. Patients taking the drug experienced an increased sense of well-being out of proportion to the degree of improvement of their lung lesions.

MACDONALD, Pittsburgh.

CLINICAL STUDY OF THE USE OF PARA-AMINOSALICYLIC ACID IN THE TREATMENT OF PULMONARY TUBERCULOSIS. ROSE I. L. DONALDSON, Edinburgh M. J. **56**:245 (June) 1949.

On the basis of three months of treatment in 10 cases of tuberculosis, Donaldson concludes that paraaminosalicylic acid may slow down the advance of tuberculosis but does not permanently halt it.

MACDONALD, Pittsburgh.

TOXOPLASMA MENINGO-ENCEPHALITIS IN LATE CHILDHOOD. O. D. FISHER, Great Ormond Street J. **1**:43 (June) 1951.

A case of Toxoplasma meningoencephalitis in a 7½-year-old boy is discussed. Nine cases in the literature are reviewed. The infection may simulate meningitis or intracranial tumor. Treatment with sulfonamides and penicillin does not appear to influence the disease, and many patients apparently recover spontaneously. Compliment fixation tests and skin tests are of value in establishing the diagnosis.

MCGUIGAN, Evanston, Ill.

TYPHOID FEVER IN CHILDREN. K. M. SUKHTANKAR, J. Indian M. A. **19**:29 (Nov.) 1949.

The treatment of typhoid in 25 children is outlined. The author favors full diet plus penicillin and sulfathiazole therapy. The declining death rate is attributed to these drugs plus a more adequate diet. Complications are fewer than in previous years.

MCGUIGAN, Evanston, Ill.

FREQUENCY OF ACUTE SEVERE TUBERCULOSIS IN CHILDREN WITH AND WITHOUT BCG VACCINATION. K. FRANK, Acta pædiat. **39**:115, 1950.

The cases of basal tuberculosis which were observed occurred in only 17.7% of the BCG-inoculated children. After inoculation half of the inoculated children lived for a relatively long period of time with people who had open tuberculosis. Although 95% of the population was tuberculin-tested, and the majority of those with negative reactions were inoculated, nevertheless, 46.7% of the cases of meningitis occurred among the infinitesimal number of children who eluded the tuberculin tests and the inoculation prescribed by the authorities.

Among the patients with severe acute pulmonary tuberculosis treated with streptomycin, only 14.8% were BCG-inoculated.

It has been shown that the majority of inoculated children who nevertheless contracted meningitis or acute miliary tuberculosis were exposed after the inoculation to massive familial infection.

FROM THE AUTHOR'S SUMMARY.

PLASMA LIPASE IN HEALTHY AND TUBERCULOUS CHILDREN AS AFFECTED BY PARAAMINOSALICYLIC ACID. L. BASSI, Lattante **22**:5 (Jan.) 1951.

The lipase content of the blood in children with pulmonary tuberculosis is subnormal. It returns to a normal amount when paraaminosalicylic acid therapy is given. When paraaminosalicylic acid in similar dosage was given to normal children, there was no quantitative change in the blood lipase levels. A combination of paraaminosalicylic acid and streptomycin had an effect similar to that of paraaminosalicylic acid alone.

HIGGINS, Boston.

TOLERANCE OF CHILDREN TO PARAAMINOSALICYLIC ACID. MARGHERITA RICCARDI and G. CORDA, Pediatria **57**:899 (Nov.) 1949.

The effect of paraaminosalicylic acid and its sodium salt were tested in children receiving treatment for tuberculosis. No striking changes were noted in the blood chemistry—protein, sodium, chloride, alkali reserve—as a result of the medication. The conclusion is drawn that the drug is well tolerated; it is felt that the sodium salt is preferable to the acid.

HIGGINS, Boston.

CASE OF TUBERCULOUS MENINGITIS CURED BY STREPTOMYCIN. THOMAS HERRERA, Acta pediat. españ. **89:** (May) 1950.

The author reports the case of a girl with definite tuberculosis: all the laboratory findings were positive, and there was a highly positive family history of tuberculosis. Treatment with streptomycin was begun at the age of 10 years, and for over a year now the child has been well and shows no sequelae of the disease or of the treatment with streptomycin. She has recovered from a minor bout with influenza in the year and passed puberty without any recurrence of the tuberculosis.

This child was one of four whom the author treated and reported on previously. One of the other children received sufficient treatment and did not return for any supervision, and in the other two encephalitis developed and death followed.

ALLEN, Santa Fe, N. M.

SUPERIMPOSED INFECTIONS IN THE COURSE OF STREPTOMYCIN TREATMENT OF TUBERCULOUS MENINGITIS. ANSELMO CALAMARI, Riv. clin. pediat. **48**:235 (April) 1950.

The author, basing this study on personal observation of two cases of purulent meningitis from Gram-positive Diplococcus occurring during streptomycin treatment of tuberculous meningitis, draws attention to the frequency of such infective complications and to the practical importance of their exact knowledge. The timely therapeutic intervention with antibiotic and sulfonamide therapy achieves the recovery of patients who would otherwise die.

FROM THE AUTHOR'S SUMMARY.

HEMOPTYSIS IN TUBERCULOSIS IN CHILDREN. NORMAN MOLL, RAUL MATTE L., and SERGIO IBANEZ, Rev. chilena pediat. **21**:22 (Jan.) 1950.

Forty cases of hemoptysis were considered from the point of view of etiology, mortality, and treatment. Twelve patients died. All had lung tuberculosis.

The complications which appeared during the onset of the disease because of the hemoptysis are analyzed; some patients died during the hemoptysis; more patients showed roentgenological and clinical indication of a posthemoptysic dissemination; in most of the cases this was due to the blood being sprayed through the bronchi.

The most useful methods of treatment of hemoptysis are collapse, pneumothorax, or phrenoplegia. The indications for any of these methods generally depend on the kind of lung lesions rather than on the quality of hemoptysis. Among the patients whose treatment did not include collapse, the percentage of failure was very high (61%).

FROM THE AUTHORS' SUMMARY.

ATYPICAL SEDIMENTATION REACTIONS IN CHILDHOOD TUBERCULOSIS. HANS SCHUERMANN, Arch. Kinderh. **135**:85, 1948.

Regularly repeated erythrocyte sedimentation rate determinations may show variations from day to day which cannot be explained by clinical findings. A normal sedimentation rate was rarely found in cases of active tuberculosis. Increased sedimentation rate and positive tuberculin skin reaction without other findings do not justify the diagnosis of active tuberculosis. Highly increased values for the sedimentation rate are very rare when the clinical findings are minimal. In such cases moderate increase of the rate is the rule. Rapid return of the erythrocyte sedimentation rate to normal does not exclude active tuberculosis.

ARON, Chicago.

BCG TUBERCULOSIS PREVENTIVE IMMUNIZATION PERFORMED PERSONALLY AND BY OTHER AUTHORS. HERBERT BUSCHMANN, Arch. Kinderh. **136**:90, 1949.

On the basis of the results collected from studies of considerably more than 50,000 children, the author concludes that the method of Calmette's BCG preventive immunization has proved its efficiency, even during the war, in Germany and in France. The originally recommended oral administration is insufficient. Subcutaneous and intracutaneous (intradermal) administration of the vaccine are equally effective. To achieve complete success, repetition of the immunization at intervals of six to seven years is required. Should the previously positive intracutaneous tuberculin reaction become negative, the immunization must be repeated earlier. A general introduction of the procedure on a voluntary basis is recommended.

ARON, Chicago.

TUBERCULOUS MENINGITIS IN CHILDHOOD. STEFAN ENGEL, Deutsche med. Wchnschr. **75**:599 (May 5) 1950.

Attention is called to the difficulties involved in making an early diagnosis of tuberculous meningitis because of the method of its propagation, which usually proceeds from the choroid plexus. Consequently, by the time the diagnosis is made, the opportunity for a successful treatment with streptomycin has passed. Therefore, prophylaxis seems more important than treatment.

AMBERG, Rochester, Minn.

IMMUNIZATION AGAINST DIPHTHERIA AND SCARLET FEVER IN CHILDREN WITH TUBERCULOSIS. RUDOLPH EICKE, Monatsschr. Kinderh. **97**:86 (June) 1949.

One hundred thirty-four children with tuberculosis were given scarlet fever and diphtheria immunizations. The number of patients in whom reactivation of the tuberculous lesions developed was insignificant. It is therefore believed that tuberculosis contributes no contraindication to active immunizations against diphtheria and scarlet fever. However, it is advisable to check patients carefully clinically and roentgenologically after the injections. The immunizing doses should be as small as is compatible with successful takes.

HARTENSTEIN, Chicago.

TRANSFER OF CONGENITAL SYPHILIS TO THE SECOND GENERATION. B. VISCOROVA-KARLOVA, Pediat. listy **4**:246, 1949.

The author describes a case in which there was transfer of congenital syphilis to the second generation and reviews the literature on this subject.

FROM THE AUTHOR'S SUMMARY.

SOME OBSERVATIONS ON THE SO-CALLED COMPLICATIONS OF BCG VACCINATION. F. BLAZEK, Pediat. listy **5**:153, 1950.

A follow-up study of BCG-vaccinated children was carried out during the period of the nationwide vaccination in Czechoslovakia. Among the children under observation because they were suspected to have complications of BCG vaccination, there were some with bronchopneumonia or whooping cough, others who were vaccinated although they had previously had a primary infection, others vaccinated in the preallergic stage, and finally a group of children who, although vaccinated, became ill with manifest tuberculosis because they succumbed to a later infection. In no case could the vaccination be proved to be the source of a manifest tuberculous infection. In the overwhelming majority of cases it was impossible to demonstrate any ill effects on the health of the children attributable to BCG vaccination. A negative tuberculin reaction alone is not a sufficient guarantee that a child is free from a primary infection. But even in cases in which a child who had previously had a primary infection was vaccinated, it was not possible to show that the vaccination harmed the child. Vaccination in the preallergic stage did not appear to have any unfavorable influence on the course of the disease. Up to now tuberculosis acquired after vaccination has had a satisfactory course, but it has not shown any tendency toward quicker healing. To obtain the best results and to preserve the good reputation of BCG vaccination, it is important that only children in a good state of health be vaccinated. Also, the condition of health of the parents and incidentally of the community must be taken into consideration. Inflammatory infiltrations in vaccinated children cannot be diagnosed to be of tuberculous or nontuberculous origin by one outpatient examination. A careful follow-up of each case is necessary in order to reach a definite conclusion. It is advisable not to make a rush diagnosis of tuberculosis in vaccinated children.

FROM THE AUTHOR'S SUMMARY.

SO-CALLED COMPLICATIONS OF BCG VACCINATION. Z. HLOUSKOVA and J. HOUSTEK, Pediat. listy **5**:157, 1950.

In order to establish whether BCG vaccination had any ill effects on the health of vaccinated children, a center was organized in Prague during the period of mass intracutaneous BCG vaccination throughout Czechoslovakia in 1949. The aim of this center was to investigate

clinically all cases of illness which were considered either by parents or by physicians to be associated with the vaccination. Lymphadenitis was found in 64 children, erythema nodosum in 7, and phlyctenular conjunctivitis in 3. There were 144 children admitted with lung infiltrations, all of which turned out to be of nontuberculous origin. In 76 children the general complaints could be explained by a simultaneous intercurrent infection. In three children tuberculous changes of the lungs developed within respectively, a week, two months, and four months, and nine children were admitted to hospital with tuberculous meningitis within one to four months of vaccination. In these cases vaccination had been carried out either in children actually suffering from tuberculosis or in the preallergic stage. The authors believe their experience proves that most of the complications have no relations to the vaccination; nevertheless, thorough examination in every such case is of the greatest importance in order to prevent BCG vaccination from being discredited in the eyes of the general public. FROM THE AUTHORS' SUMMARY.

ELECTROENCEPHALOGRAM IN TUBERCULOUS MENINGITIS. J. LESNY and J. HOUSTEK, Pediat. listy **6**:199, 1951.

Electroencephalograms were made on 46 children with tuberculous meningitis treated with streptomycin. Fourteen children were aged 1 to 4 years, 28 from 4 to 10 years, and 4 were older than 10 years. The electroencephalograms were taken in the first month of the disease in 6 cases, in the second to fourth month in 7 cases, in the sixth to ninth month in 10 cases, and later in the others. Normal curves were found in 19 cases. From the pathological changes a generalized abnormality without focal lesions was the most frequent finding. Bilateral synchrony had usually a bad prognosis.

FROM THE AUTHORS' SUMMARY.

TUBERCULIN REACTION IN DIFFERENT PARTS OF THE SKIN AND THE SENSITIVITY IN RHEUMATOID ARTHRITIS. OLE WASZ-HÖCKERT, Acta pædiat., supp. 79, p. 1, 1950.

The author has studied the technical error in the Mantoux reaction, with attention to the injection technique and reading. Double determinations were made by injection of 0.01 mg. of old tuberculin in the skin of the back in 82 tuberculous patients, and the mean error of 15% was obtained. Different methods of measuring were tested (Petranyi's modification and the usual perpendicular measuring), and it was found that the method generally used was quite reliable. The results were further checked by planimeter determinations.

The relation of the part of the skin receiving the injection to tuberculin sensitivity was studied, and the following observations were made: Mantoux tests in identical parts of the skin gave reactions of the same size (82 patients). If the anatomical difference between two sites tested was small (forearm, volar and dorsal sides) a slight difference was found (36 patients). No difference was observed between reactions in the skin on the back and those on the arm in children (109 patients). In adults, however, there was a marked difference (126 patients): The reaction in the skin on the back was much stronger than that on the arm. Tuberculin injections repeated after 14 days in adult tuberculous patients (41 patients) gave stronger reactions.

The author also studied tuberculin sensitivity in patients with rheumatoid arthritis, with the following results: Allergic reaction to 0.01, 0.001, and 0.0001 mg. of old tuberculin was stronger in tuberculous patients (130 patients) than in healthy people (130 cases); the weakest reactions were observed in patients with rheumatoid arthritis (125 patients). Harmless, secondary infections in the upper respiratory passage did not affect the tuberculin sensitivity.

FROM THE AUTHOR'S SUMMARY.

CONTRIBUTION TO THE PATHOLOGIC ANATOMY OF TOXOPLASMOSIS. JAN MELLGREN, Svenska läk.-tidning. **45**:341 (Feb. 20) 1948.

Toxoplasma was histologically demonstrated in the placenta of a stillborn premature infant with typical toxoplasmotic cerebral lesions. The mother had a positive neutralization reaction.

WALLGREN, Stockholm, Sweden.

IMPORTANCE OF THE SEVENTY-TWO-HOUR READING OF THE MANTOUX TEST. LILIAN JONSSON and BERTIL R. MALMGREN, Svenska läk-tidning. **45**:1362 (July 9) 1948.

Sixty-two of 5,523 noninfected and non-BCG-vaccinated children examined 48 hours after injection of 1 mg. of tuberculin displayed reactions of a 10 by 10 mm. area of erythema with infiltration, generally considered as a positive reaction. It is concluded that the reading of the Mantoux test after only 48 hours gives rise to false evaluations of the specificity of the reaction.

WALLGREN, Stockholm, Sweden.

TUBERCULOUS INFECTION FROM A DOG. S. URWITZ, Svenska läk.-tidning. **45**:1927 (Oct. 8) 1948.

The environmental investigation in five cases of recent primary tuberculosis, occurring in the spring of 1948 in three children and two adults, all of them living in a house within a military camp, revealed as the only demonstrable source of infection a pet dog that was suffering from pulmonary tuberculosis of human type. The dog was probably infected by a man with open pulmonary tuberculosis who in July, 1947, had often played with him. At the Veterinary School in Stockholm, postmortem examinations in 1938-1947 of 3,673 dogs revealed that 52 had tuberculosis.

WALLGREN, Stockholm, Sweden.

CASES OF PRIMARY TUBERCULOSIS AT THE CHILDREN'S HOSPITALS IN STOCKHOLM. SIGVARD JORUP, Svenska läk.-tidning. **45**:2293 (Nov. 26) 1948.

In the period 1945-1948 there were 671 children less than 15 years old who were treated for primary tuberculosis in the four children's hospitals of Stockholm. Of these, 25 (3.7%) died; 110 of the children were infants aged 0 to 24 months, and of them, 12 (10%) died. Only five of the 671 children had been BCG-vaccinated, and they suffered from a very mild type of tuberculosis. The author recommends a general BCG-vaccination, preferably in the newborn period while the infants still are at the maternity hospital.

WALLGREN, Stockholm, Sweden.

STREPTOMYCIN TREATMENT OF TUBERCULOUS MENINGITIS. GUNNAR LINDGREN and BJÖRN SJÖGREN, Svenska läk.-tidning. **45**:2449 (Dec. 17) 1948.

The authors report 54 cases of tuberculous meningitis in children and adults who were treated with streptomycin. The total mortality rate was 59%; in five cases the disease was arrested, and in the other cases the patients are still living and still under treatment, with either improved or unchanged disease.

WALLGREN, Stockholm, Sweden.

CASE OF CONGENITAL TOXOPLASMOSIS. IB BOESEN, Ugesk. læger **110**:226 (Feb. 26) 1948.

Boesen reports a case of congenital toxoplasmosis in a girl who was at examination 4 years old. At the age of 10 weeks microphthalmia and retinal lesions were found; at 1 year of age intracranial calcifications were demonstrated. She had had convulsions since 3 years of age. The girl was microcephalic and imbecilic. Neutralization tests on the mother's and the child's sera showed positive reactions.

WALLGREN, Stockholm, Sweden.

SOME CASES OF CONGENITAL TOXOPLASMOSIS. EJLER HOLM, Ugesk. læger. **110**:1363 (Nov. 25) 1948.

Holm reports two cases of congenital toxoplasmosis in Danish children, aged 2 months and 7 years, with signs of retinochorioditic lesions, intracranial calcification, and positive neutralization reaction.

WALLGREN, Stockholm, Sweden.

NOCARDIOSIS. F. KUIPERS, Maandschr. kindergeneesk. **17**:257, 1949.

The recent literature regarding nocardiosis is reviewed. The importance of vigorous treatment with modern antibiotics is stressed; also, the increasing significance of the disease in childhood is mentioned.

FROM THE AUTHOR'S SUMMARY.

Diseases of Blood, Heart and Blood Vessels, and Spleen

COOLEY'S ERYTHROBLASTIC ANEMIA: SOME SKELETAL FINDINGS IN ADOLESCENTS AND YOUNG ADULTS. JOHN CAFFEY, Am. J. Roentgenol. **65**:547 (April) 1951.

Four cases of familial erythroblastic (Cooley's) anemia followed from 11 to 20 years are presented. Characteristically, the swelling, cortical atrophy, and coarse porous rarefaction of the bones of the distal skeleton which are present during childhood regressed after puberty. Similar changes in the bones of the skull, spine, and pelvis persisted or progressed after puberty into adult life. This pattern is consistent with the regression of activity of the red marrow in the distal portions of the skeleton. Retarded pneumatization of any or all of the paranasal sinuses and the temporal bones is a frequent finding in familial erythroblastic anemia.

HODGSEN, Rochester, Minn.

SURGICAL TREATMENT OF CONGENITAL PULMONARY STENOSIS. WILLIS J. POTTS, Ann. Surg. **130**:342 (Sept.) 1949.

Shunting blood to the lungs for the relief of cyanosis due to congenital pulmonary stenosis is at present an accepted surgical procedure. The incapacitated child with a typical tetralogy of Fallot who has an elevated red blood cell count, a normal or boot-shaped heart, a systolic murmur at the base of heart, clear lung fields, and deviation of the axis to the right in the electrocardiogram can almost always be relieved by surgery.

Preoperative care is important. All cyanotic children are admitted to the hospital 48 hours before operation. Operation is contraindicated in the presence of upper respiratory tract infections. Penicillin in 100,000-unit doses is given twice daily. Apprehensive children are given sedation one hour before operation. Morphine and atropine are given to children under 5 years of age and morphine and scopolamine to all patients over 5 years of age. The author prefers cyclopropane anesthesia. He believes that cooling the patients during operation is beneficial because it lessens oxygen consumption.

The technique of aortic pulmonary anastomosis and subclavian-pulmonary anastomosis is outlined in detail.

After the operation the patient is placed in an oxygen tent for 24 hours. For a week following operation 100,000 units of penicillin is given twice daily.

The results in 135 patients who survived aortic pulmonary anastomosis and in 14 patients who survived subclavian pulmonary anastomosis have been satisfactory. However, it is still too early even to guess intelligently the future of these children.

BANTIN, Omaha.

FAVISM IN TWO CHILDREN IN CALIFORNIA. ALVIN H. JACOBS, Pediatrics **6**:51 (July) 1950.

Favism is an acute hemolytic episode with fever and malaise followed by hemoglobinuria, jaundice, and severe anemia, resulting from the inhalation of the pollen or ingestion of the bean of Vicia fava. The disease is most prevalent in Italy and Sicily; however, seven cases have been reported in the United States. This report adds two more cases occurring in children in California, where the fava bean, or broad bean, is becoming popular as an item of food.

FROM THE AUTHOR'S SUMMARY.

MEGALOBLASTIC ANEMIA IN INFANCY. D. A. J. WILLIAMSON, Great Ormond Street J. **1**:22 (June) 1951.

A case of megaloblastic anemia in a 6-month-old breast-fed infant is discussed. Treatment with folic acid resulted in permanent cure. The literature is briefly reviewed.

MCGUIGAN, Evanston, Ill.

PURPURA FULMINANS WITH DEFICIENCY OF FACTOR V. C. Gasser and G. DE MURALT, Helvet. paediat. acta **5**:364 (July) 1950.

Gasser and de Muralt present two cases of severe purpura fulminans following scarlet fever in a 7-year-old girl and in a 6-year-old boy. The clinical picture, the pathogenesis, and the therapy of purpura fulminans are discussed, and the following points are emphasized:

In the authors' cases of purpura fulminans a severe disturbance of coagulation existed which was due to an acute insufficiency of Owren's factor V, which was combined in one case with an excess of antithrombin of the heparin-antithrombin type.

The great increase of plasma cells of the reticulum and of eosinophiles in bone marrow, as well as the increase of gamma globulins in the blood as shown by electrophoresis—findings which, too, were made for the first time—point to an increased production of antibodies and to an allergic diathesis.

The second patient could be saved when moribund by a complete blood exchange transfusion, while repeated smaller transfusions for the first patient were unsuccessful. Exchange transfusion alone assures complete removal of abnormal products and a sufficient supply of those products which were absent in the blood. Exchange transfusion appears to be the method of choice for the treatment of purpura fulminans.

FROM THE AUTHORS' SUMMARY.

CASE OF APLASTIC ANEMIA. M. LATO, Minerva pediat. **1**:398 (Nov.) 1949.

A 10-year-old girl with aplasia of the bone marrow had a complete remission lasting two months following streptomycin therapy; then the aplastic condition returned, and the child died.

HIGGINS, Boston.

ACUTE LEUKEMIA WITH TUMORS SHOWN BY ROENTGENOGRAM EXTENDING THE WHOLE LENGTH OF THE DIGESTIVE TRACT. E. COMOLLI, Minerva pediat. **1**:401 (Nov.) 1949.

A 10-year-old girl with leukemia was found by roentgen examination to have multiple small tumors along the entire gastrointestinal tract. The exact variety of leukemia could not be established. It is quite possible that the tumors may be the beginning of lymphosarcomas or reticuloendotheliomas.

HIGGINS, Boston.

CASE OF HAND-SCHÜLLER-CHRISTIAN DISEASE. G. COCOZZA, Pediatria **57**:923 (Nov.) 1949.

A 2-year-old child presented tumors of the parietal bone and tumors above the orbit; biopsy revealed the tumors to be xanthomatous. The blood cholesterol was normal, and there was neither exophthalmos nor diabetes insipidus.

HIGGINS, Boston.

SERUM PROTEINS DURING RETICULOCYTE CRISIS. M. ZELENKA and K. SCHREIER, Monatsschr. Kinderh. **98**:1 (Jan.) 1950.

No correlation was found between increase in reticulocytes and serum proteins.

HARTENSTEIN, Madison, Wis.

ARTIFICIALLY INDUCED LOCAL ANOXAEMIA IN THE TREATMENT OF CHILDREN'S ANAEMIA. EVA BONSDORFF and ESTER SELESTE, Acta pædiat. **37**:441, 1949.

Nine anemic children were treated with local venous anoxemia induced by obstructing the venous circulation in a limb for one hour. In most patients the treatment caused an improvement in the red blood cell picture which in some cases lasted for some months and had a favorable effect on the general condition.

FROM THE AUTHORS' SUMMARY.

PYRUVIC ACID (P.U.) CONTENT IN THE BLOOD IN CONGENITAL HEART DISEASE. C. E. RÄIHÄ and H. TALLQVIST, Acta pædiat. **37**:449, 1949.

The writers have found high pyruvic acid values in the blood of five patients with congenital cardiac defects of the type of Fallot's tetralogy (4.2 to 8.8 mg. per 100 cc. of blood).

The pyruvic acid analyses were performed according to the method of Friedemann and Haugen, with benzene as solvent and 2,4-dinitrophenylhydrazine as color reagent.

It is claimed that these high values are a result of disorders in the carbohydrate metabolism induced by chronic anoxemia in these patients.

FROM THE AUTHORS' SUMMARY.

ISOLATED INTERSTITIAL MYOCARDITIS OF UNKNOWN ETIOLOGY. P. BASTRUP-MADSEN, Acta pædiat. **40**:85 (March) 1951.

Three cases of acute interstitial myocarditis of unknown etiology in infants are reported. In all three cases the disease manifested itself by progressive cardiac insufficiency with poor general condition, dyspnea, cyanosis, tachycardia, and an enlarged liver. The disease terminated fatally in the course of four to eight days. In all three cases autopsy revealed an enlarged soft and flabby heart and signs of congestive heart failure. In the first two cases microscopic examination showed diffuse interstitial cellular infiltration in the myocardium. Microscopic examination was not done in the third case. No foci which might be regarded as the cause of the myocarditis were found.

FROM THE AUTHOR'S SUMMARY.

AMINOPTERIN THERAPY IN LEUKEMIA IN CHILDHOOD. T. JERSILD and S. MEHLSEN, Acta pædiat. **40**:127 (March) 1951.

A survey is given of the effect of folic acid antagonists on acute leukemia in childhood. Mention is made of the chemistry, toxicity, and action of 4-aminopteroylglutamic acid ("aminopterin"). Two patients with stem cell leukemia treated with 4-aminopteroylglutamic acid are reported. For one of them no blood transfusion was given at the same time. Complete remission, clinical as well as hematological, was obtained in both cases. The drug appears to be just as effective when given by mouth as when given parenterally. One of the patients is still receiving treatment. It is emphasized that 4-aminopteroylglutamic acid may produce complete remission but not recovery.

FROM THE AUTHORS' SUMMARY.

ACUTE FORM OF GAUCHER'S DISEASE IN THREE CHILDREN IN ONE FAMILY. L. STRENGERS, Maandschr. kindergeneesk. **17**:237, 1949.

Strengers describes a case in which three children of one family had the acute form of Gaucher's disease. Investigation of the family revealed a myeloid leukemia in the father.

Splenectomy was performed on the youngest child without obvious success.

FROM THE AUTHOR'S SUMMARY.

Diseases of Nose, Throat, and Ear

PENICILLIN THERAPY OF OCCULT MASTOIDITIS WITH ACUTE DIGESTIVE DISTURBANCE. K. WEISSE, Ztschr. Kinderh. **66**:121, 1948.

Occult mastoiditis following acute infections in infants and characterized by rapid loss of weight, vomiting and diarrhea, and toxic appearance of the child was commonly treated by operation. The author treated eight patients with these symptoms and the clinical diagnosis of mastoiditis with penicillin and effected a rapid recovery of the patients. The author bases the diagnosis on the above symptoms and her clinical experience with 46 previously reported cases (*Ztschr. Kinderh.* **65**:4, 1948) in which either surgery or autopsy confirmed the diagnosis of mastoiditis in 41 of the cases.

GLASER, Chicago.

TUBERCULOSIS OF TONSILS. BANHIDY FERENC, Paediat. danub. **6**:171 (Sept.) 1949.

Removed tonsils and adenoids of 300 children between the ages of 3 and 16 years were examined for evidences of tuberculosis. Microscopic examination revealed tuberculous changes in 28 tonsils (8.4 %) and 12 adenoids (4 %). There are no symptoms which would definitely point to tuberculosis of the tonsils. Certain signs might, however, be characteristic of the condition, and these are discussed in detail. After removal of the diseased tonsils spread of tuberculosis was never observed, and recovery was uneventful in all cases.

FROM THE AUTHOR'S SUMMARY.

TONSIL PROBLEM IN CHILDREN. K. BERG, Nord. med. **37**:633 (March 27) 1948.

A follow-up study was made on the state of health of 1,717 children on whom tonsillectomy had been performed during a 10-year period. In nonallergic children with recurring tonsillitis

the effect of the operation had been very good, most of them being rid of their troubles. Considerable improvement was also found in children with frequent chills accompanied by cough and sneezing. The improvement applies to the first few years; the later results were less satisfactory. In the allergic children the results were not satisfactory; a great many of them did not show any improvement at all. In children with recurring otitis there had been obvious benefit from the operation, but adenotomy would probably have been just as useful. The relation between the tonsils and some of the common epidemic diseases was investigated, and it was found that scarlet fever incidence is markedly reduced in children who have had their tonsils removed as compared with children who still have their tonsils. In other specific infections there was no such effect.

WALLGREN, Stockholm, Sweden.

Diseases of the Lung, Pleura, and Mediastinum

PULMONARY CALCIFICATIONS? HAMARTOMATA. S. D. V. WELLER, Great Ormond Street J. **1**:57 (June) 1951.

A 7½-year-old boy was referred because of abdominal pain. No cause was found for the pain, but roentgen examination of the lungs showed many calcified foci. Tests for tuberculosis, histoplasmosis, coccidiosis, and toxoplasmosis showed negative results. No other foci were found in the body. It is suggested that the shadows were cast by hamartomas.

MCGUIGAN, Evanston, Ill.

TRILOBECTOMY IN TWO STAGES FOR BRONCHIECTASIS. PEDRO LARGHERO YBARZ and JOSE PEDRO IBARRA, Arch. pediat. Uruguay **22**:91 (Feb.) 1951.

A case of trilobectomy performed in two stages on an 11-year-old girl is presented. It was performed because of the occurrence of bronchiectasis after the inhalation of a extraneous body ("celluloid beak of a toy duck") at the age of 7 years. The accident did not at the time cause any phenomena of bronchial obstruction. A month later an acute pleuropulmonary syndrome appeared, with purulent sputum. Since then there has been pulmonary suppuration of the bronchial tree of the right lung lower and middle lobes and of the posterior part of the lower lobe of the left lung. The lingula was not affected. First the right lung lower and middle lobes were resected, and a year later the posterior part of the left lower lobe was resected. The pathological examination showed the characteristics of an abscessed bronchiectasis. The girl recovered completely, without any clinical functional deficit of the lung, even though the values of the functional respiratory study done 20 days after the second operation showed a marked insufficiency of ventilation and hemoptysis.

FROM THE AUTHORS' SUMMARY.

OCCURRENCE OF FATTY SUBSTANCES IN THE LUNGS OF INFANTS. R. GÄDEKE, Ztschr. Kinderh. **66**:183, 1948.

Microscopic examination by means of special staining methods proved the presence of fat substances in the lungs of infants. They were found more frequently during the first weeks of life and appeared enclosed in phagocytes, or as free fat globules, or in the form of needle-like crystals. As a possible origin of the fat in the pulmonary tissues the author considers entrance from the blood capillaries, but he limits this mode of entry to pathologic cases. In animal experiments fats occur only in cases with injury to the alveolar wall or pathologically high blood cholesterol levels. As a second possible cause for the presence of fat he considers the formation of fat in the lung tissues, but if such were the case, one would expect a more uniform distribution. The author comes to the conclusion that frequent minute milk aspirations must be the source of the fat globules in the pulmonary tissues. The removal of these foreign substances is effected by phagocytosis and expectoration by mechanical removal through the lymph paths and by fermentive decomposition, as concluded by the presence of crystals.

GLASER, Chicago.

TREATMENT OF EMPYEMAS IN CHILDREN. G. VOUSSURE, Acta pædiat. belg. **2**:14, 1948-1949.

After a historical review and a review and description of patients treated before 1945 (before the use of penicillin), the author discusses seven cases of suppurative pleurisy caused in two

cases by pneumococci and in five cases by staphylococci. The patients were treated by daily intrapleural penicillin injections (20,000 to 100,000 units per injection). Lavage of the pleural cavity and penicillin intramuscularly were used in some cases. Six patients recovered, whereas one patient, although recovered from the pleurisy, died of otitis media and mastoiditis and athrepsia. The author concludes that with the use of penicillin surgical intervention is almost avoidable, and the prognosis of this infection has become good, with minimal sequelae of pleural scar formation. He recommends daily injections of 50,000 units of penicillin, preferably with lavage, until two or three cultures have become negative for the causative organism. Although his experience is limited to pneumococcic and staphylococcic infections, he expects similar results in streptococcic infections and in influenza bacillus infections if treatment is with streptomycin.

GLASER, Chicago.

SULFONAMIDE THERAPY IN SECONDARY PNEUMONIA. FRANZ HEINTZELMANN, Ugesk. læger **110**:458 (April 15) 1948.

Heintzelmann studied the effect of sulfonamide therapy in 642 cases of pneumonia following specific infectious diseases such as measles, whooping cough, scarlet fever, and others. Pneumonia complicating measles had a very low fatality rate, whereas pneumonia following whooping cough and scarlet fever had a high fatality rate (6 to 15%).

WALLGREN, Stockholm, Sweden.

TREATMENT OF PNEUMONIA WITH LARGE SINGLE DOSE OF SULFATHIAZOLE IN THE LIGHT OF 688 CASES. KNUD WILKEN-JENSEN, Ugesk. læger **110**:462 (April 15) 1948.

The author reports on 638 patients with acute pneumonia and 50 with capillary bronchitis treated with large single doses of sulfathiazole. Of the pneumonia patients, 21 died (3.3%). Of these, 10 had congenital heart malformations and/or were premature infants or had Mongolism. If those who died within the first 24 hours are excluded, seven fatalities remain, giving a 1.1% mortality. Of the 50 patients with capillary bronchitis, eight (16%) died, six within the first 24 hours. The author concludes that the single massive dose treatment of acute pulmonary infection is easier, cheaper, and more time saving than the ordinary treatment with repeated doses, and it can at once be given by the physician himself. The children get more rest and become less nauseated.

WALLGREN, Stockholm, Sweden.

TREATMENT OF ASTHMATIC CHILDREN AT A SEASIDE HOSPITAL. SVEN HELBO, Ugesk. læger **110**:1287 (Nov. 11) 1948.

About one-third of the asthmatic children will become free from attacks after specific desensitization at home, and a large proportion of the others may be cured by climatic treatment. At the seaside hospital, where the author works, about 80% of admitted children became free from asthmatic attacks, and 50% of these remain free after their return home.

WALLGREN, Stockholm, Sweden.

SYMPATHICOGONIOMA WITH PECULIAR METASTATIC LOCALIZATION. J. SLOOFF, Maandschr. kindergeneesk. **19**:319 (Oct.) 1951.

A description is given of a sympathicogonioma situated in the anterior mediastinum in a boy aged 4 years. Expansive growth was found around the trachea and in the thyroid. Metastatic growth was found only in both kidneys.

FROM THE AUTHOR'S SUMMARY.

Diseases of Gastrointestinal Tract, Liver, and Peritoneum

POLYPS OF THE COLON. C. E. BOYD, New Orleans M. & S. J. **104**:92 (Sept.) 1951.

Polyps of the colon occur rarely in children, and when they do, they are usually single and pedunculated. In children who pass fresh blood by rectum, and in children who have this complaint, one of four will be found to have a polyp.

MCGUIGAN, Evanston, Ill.

LABORATORY DIAGNOSIS OF CYSTIC FIBROSIS OF THE PANCREAS. D. E. JOHNSTONE and E. NETER, Pediatrics **7**:483 (April) 1951.

A study of 78 patients with cystic fibrosis of the pancreas was carried out to determine whether gelatin-liquefying bacteria may be responsible for gelatin liquefaction of gelatin film (the roentgenogram film used in routine practice) by feces and duodenal juice. In addition, the records of 254 children with cystic fibrosis of the pancreas were reviewed relative to the incidence of apparently false positive gelatin film reactions. The following data were obtained:

1. Fecal specimens of 48 of 78 patients yielded positive gelatin film reactions. Only nine of these 48 specimens showed positive reactions in a dilution of 1:25 or higher, but 33 gave positive reactions in a dilution of 1:10. Likewise, a review of 254 charts of proved cases of cystic fibrosis revealed that of 131 tests on 59 patients 71, or 54%, showed positive reactions.

2. Gelatin-liquefying bacteria were present in the feces of 44 of 45 patients whose stool specimens gave a positive gelatin film reaction and which also were examined bacteriologically, but in only two of 28 whose feces gave negative gelatin film reactions.

3. Treatment with penicillin may be associated with an increase in the percentage of positive gelatin film reactions. Of 42 patients whose feces were obtained prior to or without penicillin therapy, only four gave positive gelatin film reactions, whereas the feces of 55 of 80 patients who had received treatment with penicillin did so.

4. Soy bean trypsin inhibitor partially or completely prevented gelatin liquefaction by fecal specimens of patients with cystic fibrosis of the pancreas only if the latter were diluted to 1:5 or less, possibly indicating the presence of small amounts of trypsin. This titer of soy bean trypsin inhibitor-neutralizable enzyme is far below normal.

5. Gelatin-liquefying bacteria were found in all 10 of the cultured duodenal juice specimens which gave apparently false positive gelatin film reactions in a dilution of 1:10 or higher.

6. The incidence of gelatin-liquefying bacteria in the throat and feces of patients giving apparently false positive fecal gelatin film reactions was far greater in the penicillin-treated patients than in untreated patients.

7. The importance of the apparently false positive gelatin film reaction is discussed, and modifications of this test are outlined which make for greater reliability.

FROM THE AUTHORS' SUMMARY.

STUDIES IN STEATORRHEA. A. W. CHUNG, SOLEDAD MORALES, SELMA E. SNYDERMAN, J. M. LEWIS, and L. E. HOLT JR., Pediatrics **7**:491 (April) 1951.

The authors studied the effect of the level of dietary fat upon the absorption of fat and other foodstuffs in idiopathic celiac disease and cystic fibrosis of the pancreas. Metabolic observations were carried out on three patients with "idiopathic" celiac disease and three patients with cystic fibrosis of the pancreas at different levels of fat intake. It was found that fat absorption remained proportional to fat intake even at high levels. Increasing the intake thus led to improved absorption. Deleterious clinical or metabolic effects were not encountered, with one possible minor exception. The implications of these observations are discussed.

FROM THE AUTHORS' SUMMARY.

PNEUMATOSIS INTESTINALIS. ELLEN P. MACKENZIE, Pediatrics **7**:537 (April) 1951.

Thirteen cases of pneumatosis intestinalis are reported, 12 of them in infants between 12 days and 12 months of age, one in a boy of 6 years. Review of these cases and of 32 reported cases falling within the pediatric age range discloses that the disease occurs most frequently in patients whose general condition is poor, that it is very often associated with congenital or acquired disease of the intestine, and that respiratory disease, usually infectious, frequently coexists. The presence of pneumatosis in pediatric patients has so far been discovered only at autopsy, but clinical diagnosis, with the aid of the typical roentgenologic findings, is feasible and may be accomplished when the disease is more widely known.

The clinical picture and roentgenographic findings in adults are reviewed. The most acceptable theories concerning the pathogenesis are discussed, with their possible relation to infantile diarrhea.

FROM THE AUTHOR'S SUMMARY.

CONGENITAL OBSTRUCTIONS OF THE ALIMENTARY TRACT IN INFANTS AND CHILDREN: ERRORS OF ROTATION OF THE MIDGUT. FREDERIC N. SILVERMAN, and JOHN CAFFEY, Radiology **53**:781 (Dec.) 1949.

Congenital obstructive lesions of the alimentary tract are largely the result of two basic embryologic faults: (*a*) failure of recanalization of the lumen (intrinsic obstruction) and (*b*) errors in deposition of the midgut section (extrinsic obstruction). Atresias and stenoses occur in all parts of the alimentary tract. Atresias occur with greater frequency in the ileum and also are manifest in the first days of life. Stenoses are found more frequently in the duodenum and may be asymptomatic until some precipitating factor causes the obstruction to become complete. The passage of meconium is no assurance of patency, as meconium may be formed below the site of complete obstruction. Tests for bile or cornified epithelial cells may be helpful.

Roentgenographic findings of dilatation and hypertrophy, often with air and fluid levels above the obstruction, offer most help in diagnosis. Errors of rotation of the midgut may be present for years before complete obstruction supervenes. Incomplete obstruction can never be excluded when air is evidence of malposition or abnormal mobility of the cecum. Clinical symptoms are likeliest to be due to volvulus, peritoneal bands, or the presence of other organs. Ectopia of the cecum is a distinctive finding.

ANSPACH, Chicago.

LIVER FUNCTION TESTS IN INFANCY. S. D. V. WELLER, Great Ormond Street J. **1**:26 (June) 1951.

Results of liver function tests in 53 infants with biliary disease were reviewed and correlated with clinical and pathological studies in each case. The author concludes that the Takata-Ara, thymol turbidity, alkaline phosphatase, and van den Bergh tests are of no material value in the first year of life, and that even all four together are of less value than the clinical impression of the case.

MCGUIGAN, Evanston, Ill.

ACHOLURIC JAUNDICE IN INFANCY. G. H. NEWNS, Great Ormond Street J. **1**:32 (June) 1951.

A survey of patients with acholuric jaundice seen at the Great Ormond Street Hospital over 10 years revealed that nearly 50% had symptoms during the first year of life. It is suggested that the manifestations of the disease in infancy are much commoner than supposed. Repeated red cell fragility tests should be carried out in cases of neonatal jaundice without Rh incompatibility. Search for presence of the disease in siblings should also be made. Those children who have symptoms in the first two years should be considered for splenectomy early in life.

MCGUIGAN, Evanston, Ill.

HERNIA IN CHILDREN. U. C. CHAKRABORTY and P. C. SARKAR, Indian J. Pediat. **18**:15 (Jan.) 1951.

The problem of hernia in children is discussed, and treatment is outlined. Surgery is the treatment advised. In young children patients are kept in the hospital only two to three hours postoperatively.

MCGUIGAN, EVANSTON, ILL.

EPIDEMIC HEPATITIS IN INFANCY WITH SPECIAL REGARD TO DIFFERENTIAL DIAGNOSIS. ANDRE MEAN, Ann. pædiat. **176**:225 (April) 1951.

A description is given of epidemic hepatitis in infancy (clinical picture and morbid anatomy after investigation of 13 cases of jaundice in infants and in one boy of 2 years). There is a discussion of the differential diagnosis, especially of serum hepatitis. At the same time, three other rare cases of jaundice are described: one case of mechanical icterus caused by an inflammatory swelling of the papilla of Vater, one case of hepatic fibrosis, and one of cirrhosis of the liver after toxic enteritis. The importance of the relation between epidemic hepatitis and toxic enteritis is emphasized. The anatomic changes caused by epidemic hepatitis in infancy were demonstrated in five cases; they do not differ from those found in older children.

FROM THE AUTHOR'S SUMMARY.

X-Ray Diagnosis in Abdominal Pain in Children. F. Gierthmuhlen, Ann. pædiat. **176**:327 (May) 1951.

Abdominal pains in infancy without clear clinical findings can often be explained by radiological investigation. The following causes are found: pangastritis, antrum gastritis, gastroduodenitis, enteritis of various origins, Ascaris, specific and nonspecific affections of the small intestine, adhesions of the appendix, specific diseases of the colon, and flatulence. The chronic form of Crohn's disease and enteritis regionalis non stenosans is pointed out, and the importance of radiological examination of the small intestine.

From the Author's Summary.

The Infectious Etiology of Diarrhea in Infants. P. Ritossa, Lattante **21**:681 (Nov.) 1950.

The basis of the symptoms is discussed for each of the two types of infantile diarrhea—the parenteral and the enteral.

Higgins, Boston.

Total Transitory Regression, Both Clinical and Metabolic, in a Diabetic During the Course of Infectious Hepatitis. C. Lombroso, Minerva pediat. **1**:392 (Nov.) 1949.

In a 10-year-old boy with mild diabetes mellitus infectious jaundice developed. The blood sugar returned to normal; the urine became sugar-free, and no insulin was required during the attack of jaundice. With the clearing up of the jaundice, the laboratory and the clinical signs of the diabetes had returned. Other similar cases are reported from the literature, including one by Claude Bernard in 1877.

Higgins, Boston.

Blood and Bone Marrow Pictures in Hypertrophic Stenosis of the Pylorus. A. Grassi, Minerva pediat. **1**:412 (Nov.) 1949.

A 6-week-old boy with pyloric stenosis but otherwise normal was found on blood examination to have an increase in the white blood cell count, especially in the polymorphonuclear series, and a high color index in the red blood cells; in a bone marrow smear there were a scarcity of proerythroblasts and basophilic erythroblasts and irregular maturation of the more advanced cells of the red blood cell series. The findings in this case seem to indicate some hemoregulator function in the gastroduodenal mucous membrane.

Higgins, Boston.

Chloromycetin in Acute Enteritis in Infants. L. Nassi, Riv. clin. pediat. **47**:593 (Sept.) 1949.

Chloramphenicol (chloromycetin®) was given orally to 12 infants with acute enteric syndrome. The doses varied between 43 and 92 mg. per kilogram in 24 hours, for four to eight days, with a total dose of 2 to 4 gm. Bacteriological examinations of the feces of these patients were made during treatment with chloramphenicol. The results obtained with this treatment were very encouraging, as a rapid fall in the temperature, a return to normal of the feces, and increase of weight were noted. These results are much better than those observed by the author in similar cases in which treatment was with sulfaguanidine or streptomycin given orally. The author believes, therefore, that chloramphenicol, in conjunction with the normal hydrating and diet therapy, should be widely tried in cases of acute enteric syndrome.

From the Author's Summary.

Pneumoretroperitoneum in the Child. G. de Giuli and A. Righini, Riv. clin. pediat. **49**:81 (Feb.) 1951.

The authors describe their gaseous contrast studies of retroperitoneal spaces in children. The technique employed is described, and the present knowledge of the anatomical regions studied on the basis of the anatomoradiological findings is discussed.

From the Authors' Summary.

LATENT PYLORIC STENOSIS. ALESSANDRO BIEBER, Riv. clin. pediat. **49**:93 (Feb.) 1951.

The author presents clinical and x-ray evidence of a form, which has not previously been described and which he calls "latent pyloric stenosis." Clinical symptoms include anorexia; light, uneven, irregular vomiting (from the first week of the child's life), and stationary weight (gain 5 to 10 gm. a day). Radiological examination shows that passage of "opaque food" through the pylorus begins regularly. The passage is slow and prolonged but appears normal. The stomach is normal in shape, and normally tonic and kinetic.

Bieber discusses the differential clinical and x-ray diagnosis as regards manifest congenital pyloric stenosis and concludes that all forms of pyloric stenosis probably have a common pathogenesis. He is inclined to the theory that pyloric stenosis is a primitive form probably of nervous origin. Both the latent forms and the various forms of manifest pyloric stenosis have a common anatomic basis, even though it is microscopically insignificant.

The author stresses particularly the importance of knowledge of these latent forms which might remain undiagnosed. Among the remote consequences of therapeutic omission are retardation of the child's development, somatic hypoevolution, and actual lifelong microsomia.

FROM THE AUTHOR'S SUMMARY.

STREPTOMYCIN IN THE TREATMENT OF DIARRHEA IN INFANTS AND PREMATURE BABIES IN HOSPITALS. ALEJANDRO MANTEROLA, OSCAR UNDURRAGA, and JULIO MENEGHELLO, Rev. chilena pediat. **22**:1 (Jan.) 1951.

The results of treatment of 109 patients with diarrhea with streptomycin are reported. Seventeen cases of dystrophic babies are presented and 47 of premature babies.

Of the dystrophic patients, 18 had toxicosis and 45 had diarrhea of dysenteric type.

The drug was given in a dose of 150 mg. per kilogram of body weight; 100 mg. was given orally and 50 mg. intramuscularly. In some cases the total amount was given in divided doses. All patients received general therapeutic measures according to individual needs.

Good results were obtained in the dysenteric type of diarrhea. In toxicosis cases the authors considered that streptomycin has not altered the bad prognosis that this illness has among hospital patients. Malnutrition is an important factor and seems to be one of the principal causes of failure.

In premature babies with diarrhea prompt recovery was obtained with streptomycin therapy.

FROM THE AUTHORS' SUMMARY.

DETERMINATION OF TRYPSIN IN THE STOOLS. B. OSCAR CORREA and V. SALVADOR ROSELLO, Rev. chilena pediat. **22**:101 (March) 1951.

A study based on analysis of trypsin in the stools by the film test is reported. The work covers approximately 700 tests carried out on 230 infants and children from 0 to 5 years of age. This material included premature infants, full-term infants from 0 to 2 years, and children from 2 to 5 years, all healthy and normal; several groups of infants with mild dystrophy, atrophy, acute nutritional disturbances, rickets, bacillary dysentery, and various parenteral infections, and children from 2 to 4 years with severe malnutrition. The results of the study may be summarized as follows: 1. Both the premature and the healthy full-term infants showed positive reactions. 2. In healthy children from 2 to 5 years there was a large number of negative reactions, especially in the older groups. 3. In infants with mild dystrophy and atrophy all the tests except one were positive. 4. In infants with acute nutritional disturbances, rickets, bacillary dysentery, and various parenteral infections the test was positive in all. On the other hand, in the patients over 2 years of age with severe forms of malnutrition (cystic fibrosis of the pancreas was excluded) results were negative in a high percentage of cases.

FROM THE AUTHORS' SUMMARY.

ESOPHAGEAL BLEEDING AFTER BURNING. ERNST KAISER, Wien. klin. Wchnschr. **61**:52 (Dec. 30) 1949.

The patient, a 1½-year-old girl, died six days after being burned with hot water. The second day severe vomiting started, and on the fifth day a transfusion was given and was followed by severe gastrointestinal bleeding. On postmortem examination an unusually intense peptic esophagitis was found, with esophageal hemorrhages as a consequence.

AMBERG, Rochester, Minn.

SUPPORTING THERAPY WITH EMETINE IN SUPPURATIVE PERITONITIS IN CHILDREN. V. TOSOVSKY and V. HOLUB, Pediat. listy **6**:217, 1951.

To 30 children with perforated, gangrenous appendicitis, phlegmonous appendicitis, or peritonitis, subcutaneous injections of 0.02 to 0.03 gm. of emetine hydrochloride were given by the method of Melchior (Turkey). Other treatment (antibiotics, infusions, transfusions) was continued as usual. This is a preliminary report, but the authors consider that the effect is beneficial. Emetine has a stimulating, bactericidal, and analgesic effect and a soothing effect on peristalsis.

FROM THE AUTHORS' SUMMARY.

MECONIUM ILEUS AND HIRSCHSPRUNG'S DISEASE. T. EHRENPREIS, Acta pædiat. **40**:227 (May) 1951.

Without questioning the close connection generally accepted between fibrocystic disease of the pancreas and meconium ileus, it seems justifiable to state that some cases of meconium ileus are due to an extensive agenesis of the myenteric plexus, and that these are virtually cases of Hirschsprung's disease. In these cases secondary change in the pancreas may or may not be present. The proportion of these two types of meconium ileus cannot be settled as long as studies of the myenteric plexus in meconium ileus are rare.

FROM THE AUTHOR'S SUMMARY.

ULCERATIVE COLITIS IN CHILDREN. RUTGER LAGERCRANTZ, Nord. med. **41**:258 (Feb. 11) 1949.

A study of 134 cases of ulcerative colitis in children is presented. The cause of the disease is unknown. Psychic factors are often of importance. It is obvious that the disease is infectious in orgin. The majority of patients were periodically subfebrile and had a hypochromic anemia and lymphocytosis, and high sedimentation rate. Progressive anemia was frequent. Rectoscopy was a valuable diagnostic means, showing changes at the various stages, from a swollen, granulated mucous membrane to ulcers and scars. X-ray examination showed changes in the whole colon in about two-thirds of the cases, and in some cases also in the caudal part of the ileum. Bacteriological examination showed that cocci and hemolytic types of colon bacilli were preponderant in the stools during the acute stages. A follow-up study was carried out in 131 cases. The course of disease was markedly intermittent. Complications occurred in about one-third of the cases, the most prevalent being anemia and thrombosis. Ten patients died of ulcerative colitis or complications. Prognosis was bad in all cases with progressive anemia and changes in the whole colon. Lagercrantz emphasizes that children with ulcerative colitis should be allowed a rich and varied diet. Blood transfusions and iron bring improvement in most cases. Early treatment with chemotherapeutics is essential. The best results have been obtained with "salazopyrin" (salicyl-azo-sulfapyridine). The drug should be given in large doses over a long period.

WALLGREN, Stockholm, Sweden.

SEVERE RESPIRATORY INVOLVEMENT IN A CASE OF RESECTION OF THE INTESTINE. J. VAN LOOKEREN CAMPAGNE, Maandschr. kindergeneesk. **19**:268 (Oct.) 1951.

Celiac disease is characterized by several symptoms, one of the most marked of which is the impaired growth. It seems to be obvious that this trouble is due in part to incomplete intestinal absorption, but there are other possible explanations, e. g., primary endocrine dysfunction.

Especially in view of this difference of opinions is the case reported important. An infant girl at the age of 3 weeks underwent an operation for intestinal obstruction by mesenteric cysts, which necessitated an extensive resection of the small intestine. After this operation there developed typical celiac syndrome, with arrest of growth, voluminous gray stools with 40 to 50% fat in the dried masses, irritability of mind, poor appetite, and enhanced predisposition to infections and to deficiencies of minerals, proteins and vitamins.

The general condition and absorption of fats were favorably influenced by a diet mainly composed of grated apples to which were added such foods as dextrose, dextri-maltose,® curds of buttermilk, fruit-juices, raw beef, and boiled liver, a diet which is also very well tolerated by children with celiac disease. In spite of this therapy, however, the condition of the child very gradually went downhill, and she died at the age of 8 years of hepatic cirrhosis.

The autopsy showed that there was no more than 1 meter of small intestine left and that the ileum had been totally removed.

FROM THE AUTHOR'S SUMMARY.

Nervous Diseases

PETIT MAL EPILEPSY OCCURRING IN STATUS. WEIR TUCKER and FRANCIS FORSTER, Arch. Neurol. & Psychiat. **64**:823 (Dec.) 1950.

Two cases of frequently repeated petit mal attacks are described in which the patients were thought to have psychomotor seizures. Diagnosis was established by electroencephalograms.

McGUIGAN, Evanston, Ill.

THIRD VENTRICULOSTOMY IN TREATMENT OF OBSTRUCTIVE HYDROCEPHALUS IN CHILDREN. HAROLD C. VARIS, A. M. A. Arch. Neurol. & Psychiat. **65**:265 (March) 1951.

The author obtains encouraging results by ventriculostomy in obstructive hydrocephalus when there is no evidence of obstruction of the basilar subarachnoid cisterns.

McGUIGAN, Evanston, Ill.

PERMANENCY OF GLUTAMIC ACID TREATMENT. FREDERICK T. ZIMMERMANN and BESSIE B. BURGEMEISTER, A. M. A. Arch. Neurol. & Psychiat. **65**:291 (March) 1951.

Follow-up studies long after discontinuance of therapy indicate a considerable degree of permanence after glutamic acid therapy.

McGUIGAN, Evanston, Ill.

GANGLIONEUROMA OF THE NODOSE GANGLION OF THE VAGUS. RICHARD C. CLAY, Ann. Surg. **132**:147 (July) 1950.

Ganglioneuroma is a rare tumor in the neck. In this location it usually arises from the cervical sympathetic ganglia. Clay reports the successful removal of such a lesion from a 2½-year-old girl.

BANTIN, Omaha.

DESCRIPTION AND DIFFERENTIATION OF TYPES OF CEREBRAL PALSY. WINTHROP MORGAN PHELPS, Nerv. Child **8**:107, 1949.

This, the first and leading article of a symposium on the subject of cerebral palsy, contains an excellent clinical description of the various types of cerebral palsy. In addition to this description, other conditions commonly confused with cerebral palsy are excellently described and their differentiation made clear.

WEINFELD, Highland Park, Ill.

CEREBRAL PALSY TODAY. LYON K. LOOMIS, New Orleans M. & S. J. **102**:321 (Dec.) 1949.

Cerebral palsy is divided into five types: spastic, tremor, athetoid, rigidity, and ataxic. Treatment is briefly summarized, and its objectives are stated as to make the patient useful to society, to enable him to help himself, and to make him happier. Speech therapy, occupational and physical therapy, surgery, drugs, and psychotherapy all have their uses. The importance of the parent-child relationship is emphasized, and parents are urged to take an intensive course at the beginning in order to better understand their child and his problems.

McGUIGAN, Evanston, Ill.

SOME FUNCTIONAL NERVOUS DISORDERS IN CHILDHOOD. J. L. HENDERSON, Edinburgh M. J. **56**:129 (April) 1949.

This review discusses the backgrounds of a wide variety of functional nervous disorders of childhood. Henderson points out that heredity is the most important factor in such disorders, since it not only influences the child directly but also determines the character of his most important environmental influences, his parents. In the prevention of such disorders, a calm atmosphere of affection and mutual confidence between mother and child must be maintained. Most of these disorders can be handled by the attending physician; difficult cases may require the assistance of a child psychiatrist.

MACDONALD, Pittsburgh.

MARASMUS RELATED TO INTERNAL HYDROCEPHALUS AND AN ASTROCYTOMA OF THE THIRD VENTRICLE. S. D. V. WELLER, Great Ormond Street J. **1**:53 (June) 1951.

A 4½-year-old boy who had shown failure to gain weight and some enlargement of the head since 7 months of age was found to have an astrocytoma of the third ventricle with resulting internal hydrocephalus. Frequent admission prior to this age had failed to establish a cause for the marasmus.

MCGUIGAN, Evanston, Ill.

TREATMENT OF PNEUMOCOCCUS MENINGITIS WITH MAXIMUM DOSES OF PENICILLIN. R. GOLDSTEIN, Ann. pædiat. **177**:55 (July) 1951.

The author recommends the treatment of pneumococcal meningitis with large intramuscular doses of penicillin (8 to 12 times daily 500,000 to 1,000,000 units, total dose of 4 to 10 million units). This treatment is superior to the combined therapy of penicillin given intrathecally and intramuscularly in smaller doses with sulfonamides given orally. With this method the duration of treatment is considerably shortened. Also, the irritation of the meninges by the injected penicillin is avoided, and development of scars and of encephalitic foci is less likely.

The control of the number of cells in the spinal fluid resumes again its absolute importance; with intrathecal therapy the number of cells was slightly increased owing to the injection, and these figures could thus not be used for prognostic purposes or as an indication of when the treatment should be terminated.

Intramuscularly injected penicillin in large doses is therapeutically more reliable than intrathecally injected penicillin, because irrespective of adhesions it will reach all the inflamed regions and reduce the risk of relapses.

FROM THE AUTHOR'S SUMMARY.

CEREBRAL ABSCESS CURED BY LOCAL AND SYSTEMIC PENICILLIN THERAPY. G. GASPARI, Clin. pediat. **30**:465 (July) 1948.

An infant of 4 months had been sick for 10 days with fever. She had the Jacksonian type of convulsions, and sulfonamide therapy had not relieved the condition. Lumbar puncture yielded a clear yellow fluid with no bacteria and only one cell; the Pandy reaction was positive. A ventricular puncture through the fontanel revealed a brain abscess (staphylococcic) in the left cerebrum; 60 cc. of pus was removed On four successive days, 20,000 units of penicillin was injected into the abscess cavity. Penicillin was also given intraspinally and intramuscularly. One month later, the child's temperature was normal and the acute infection apparently cured. Development was a bit slow, but at 25 months the child was walking and saying a few words; there was slight spasticity of the muscles of the right arm and hand.

HIGGINS, Boston.

THE VALUE OF WEICHBRODT'S REACTION AND THE TEST OF GORIA. L. PERALE, Clin. pediat. **30**:500 (Aug.) 1948.

For spinal fluids from patients with meningitis, Weichbrodt's test for globulin was found to be not so sensitive as the Pandy or Nonne-Apelt tests. In spinal fluids from patients with brain tumor or with cerebral bleeding, Goria's dilution technique permitted a satisfactory comparison of the three tests, it being found that the Weichbrodt test was quite as sensitive as the Pandy and Nonne-Apelt tests.

HIGGINS, Boston.

CONGENITAL LARYNGEAL STRIDOR FROM LESIONS OF THE CENTRAL NERVOUS SYSTEM. N. GRILLO, Lattante **20**:301 (May) 1949.

A girl of 7 months had had a loud stridor since birth; she also was undernourished and had chronic mucopurulent rhinitis, inability to hold up her head, aphonia, and paralysis of the constrictor muscles of the pharynx and the palate. The basic pathologic factor is believed to be a congenital lesion of the central nervous system, probably in the nucleus ambiguus.

HIGGINS, Boston.

TREATMENT OF PURULENT MENINGITIS IN INFANCY. P. FORNARA, Lattante **20**:641 (Nov.) 1949.

Detailed therapeutic procedures and medications for the different types of purulent meningitis are presented on the basis of reports from the medical literature and the author's personal clinical experience.

HIGGINS, Boston.

EXPERIMENTAL OBSERVATIONS ON THE INTRODUCTION INTRASPINALLY OF PARAAMINOSALICYLIC ACID. C. MARINI and W. MONTORSI, Minerva pediat. **1**:384 (Nov.) 1949.

In dogs there is little or no paraaminosalicylic acid to be found either in the brain tissue or in the spinal fluid after the drug is injected into the carotid artery. When the drug is administered by cisternal puncture, it acts as an irritant, because the acidity of the spinal fluid is raised to a pH of 6.5; the drug is found in measurable quantities in the brain tissue, being higher in the cerebellum than in the cerebrum; such injections lead to unsteadiness and convulsions, often fatal; these convulsions may be somewhat controlled by sedatives. Caution is advised as to the clinical use of paraaminosalicylic acid by cisternal (or lumbar) puncture.

HIGGINS, Boston.

LATER RESEARCHES ON THE MECHANICS OF THE ACTION OF STREPTOMYCIN ON THE CENTRAL NERVOUS SYSTEM. LEONARDO DONATELLI and ARRIGO GALEOTTI FLORI, Riv. clin. pediat. **46**:775 (Dec.) 1948.

Streptomycin hydrochloride and streptomycin calcium chloride complex, administered in different ways, and also by direct application on the central nervous system, to both mammals and amphibians, has been tested. A depressing, direct action on the whole central nervous system has been evidenced with large doses; this depressing action is thwarted by strychnine, pentylenetetrazole, and picrotoxin. Streptomycin has also shown a depressing action on the peripheral neuromusculature, but such an action is produced by doses larger than those active on the central nervous system.

FROM THE AUTHORS' SUMMARY.

CEREBRAL CAPILLARY AND BLOOD ENCEPHALITIC BARRIER. GUIDO NOCCIOLI, Riv. clin. pediat. **47**:303 (April) 1949.

The author reviews the studies undertaken of the blood encephalitic barrier and outlines the anatomical and physiological layout of the cerebral capillary vessels, with an intent to show their very great importance as regards this barrier.

FROM THE AUTHOR'S SUMMARY.

SPONGIOBLASTOMA OF THE CEREBELLUM. J. A. C. DA SILVA JR., O. AIDAR, and A. M. C. DE ALMEIDA, Arq. neuro-psiquiat. **9**:73 (March) 1951.

A white Brazilian boy aged 13 was admitted to the hospital with the history of an illness of two months' duration, characterized by pains in the neck, followed soon by vomiting. There was definite progression of symptoms to the time of admission. On examination the head seemed to be enlarged; there were unsteadiness in gait and station, with cerebeller ataxia; signs on the right of involvement of the pyramidal tract; bilateral papilledema; diminution of visual acuity; dilation of the pupils, and weakness of the right side of the face. Examination of the spinal fluid showed an initial pressure of 650 mm. when the patient was in the sitting position; there were two cells per cubic millimeter, with a positive Pandy reaction and a negative Wassermann reaction. Roentgenograms of the skull showed increased digitations, separation of the sutures.

and calcification in the region of the right posterior fossa. Ventriculographic examination showed pushing of the aqueduct toward the left side, indicating a probable lesion on the right side. An inoperable tumor was observed in the region of the vermis. Autopsy showed a tumor in the region of the vermis, extending into the right hemisphere. In the right hemisphere the tumor was cystic; the cyst did not communicate with the ventricles or the subarachnoid spaces. The histologic diagnosis was spongioblastoma polare.

SAVITSKY, New York [A. M. A. ARCH. NEUROL. & PSYCHIAT.].

TREATMENT OF PURULENT MENINGITIS WITHOUT INTRATHECAL THERAPY. JOSÉ BONABA and JOSÉ M. PORTILLO, Pediat. Américas **7**:318 (July) 1949.

Nine cases of purulent meningitis of undetermined etiology were studied. The authors discuss the dangers of intrathecal therapy and propose instead therapy with combined penicillin and streptomycin given by intramuscular injection and sulfadiazine given by mouth. The amount of streptomycin recommended is 50,000 units per kilogram every 24 hours. All the nine patients recovered.

DE LA TORRE, México, D. F., México.

MENINGITIS SEROSA EPIDEMICA. R. POMÓTHY, Orvosok lapja **4**:1112 (Aug. 29) 1948.

Pomóthy observed 12 cases of meningitis serosa epidemica, in the summer of 1947, among children 2 to 14 years old. Differentiations from other forms of meningitis are discussed. Pomóthy believes that the differentiation from the meningeal form of poliomyelitis is difficult but possible. He points to the evaluation of the cell protein dissociation in the cerebrospinal fluid as in favor of poliomyelitis.

GÖRGÉNYI-GÖTTCHE, Budapest, Hungary.

ALBUMINOCYTOLOGICAL DISSOCIATION WITHIN THE CEREBROSPINAL FLUID IN A PATIENT WITH POLYRADICULONEURITIS CURED AFTER TONSILLECTOMY. A. IANCU, T. PONOVA, and D. DUMA, Paediat. danub. **4**:175 (Oct.) 1948.

The case of a 9-year-old boy with the characteristics of the Guillain-Barré syndrome is described. After the removal of diseased tonsils, recovery rapidly took place.

A review is made of the literature on the Guillain-Barré syndrome, and the rarity of its occurrence in children is mentioned. The difficulties in differential diagnosis are discussed, especially in relation to poliomyelitis and postdiphtheritic paralysis. The confusion concerning etiology of the syndrome is described. Support is given to the theory of a focus of infection by the recovery in the present instance after tonsillectomy. The independence of the syndrome as a clinical entity is maintained as justified.

A follow-up examination 10 months after the patient had been discharged showed normal sight, swallowing, and reflexes, except for the right patellar reflex, which was somewhat slow. Muscles were well developed; the child played football. The cerebrospinal fluid was normal, protein, determined according to the method of Siccard and Cantaloube, was below 15 gm. per 100 ml.

FROM THE AUTHORS' SUMMARY.

NEWLY RECOGNIZED REFLEX FOR DIAGNOSIS OF INTRACRANIAL INJURIES ENSUING DURING LABOR. I. ZADOR, Paediat. danub. **4**:256 (Nov.) 1948.

In a 2-day-old infant the attempt to elicit Troemner's reflex in the right hand resulted in extension and spreading of the fingers. At autopsy a subarachnoid hematoma was found in the lower third of the left anterior gyrus centralis. This reflex phenomenon has not been reported previously.

FROM THE AUTHOR'S SUMMARY.

LYMPHOCYTIC CHORIOMENINGITIS. Z. ERDÓS, Paediat. danub. **5**:143 (March-April) 1949.

Numerous reports on cases of serous meningitis have been published recently from various countries. There were often considerable discrepancies in the clinical pictures recorded. On the basis of data from the literature and the symptoms and course of the patient with verified lymphocytic choriomeningitis reported, the author concludes that only a few of the cases reported under the diagnosis of serous meningitis were of real viral lymphocytic choriomeningitis. In

most of the cases, especially those in which paralyses were present, the disease must have been caused by other viruses, among them, different encephalitis strains.

FROM THE AUTHOR'S SUMMARY.

OBSERVATIONS ON SURGICAL TREATMENT OF HYDROCEPHALUS IN INFANTS. M. SULAMAA, Nord. med. **41**:640 (April 8) 1949.

Sulamaa reports 42 cases of surgical treatment of hydrocephalus in infants. Three-fourths of the patients were younger than 1 year. In eight cases resection of the choroid plexus was performed; ventriculostomy was performed in three cases according to the method of Thorkildsen and in 11 cases according to the method of Dundee. Heile's operation with nephrectomy and dura and renal pelvis drainage was performed in 13 cases, with seven patients recovering. Two of these seven patients died two and one-half to five months later with signs of acute meningitis. The opinion is expressed that in the cases of "successful" surgical treatment, the process has often come to an end spontaneously, and the significance of the operation is thus doubtful.

WALLGREN, Stockholm, Sweden.

SPECIFIC TREATMENT OF HEMOPHILUS INFLUENZAE (PFEIFFER) MENINGITIS. KNUD BRÖCHNER-MORTENSEN, HANS C. ENGBAEK, and KOI SCHMITH, Ugesk. læger **110**:139 (Feb. 5) 1948.

With type-specific serum produced in Denmark, seven patients were treated; of these, two died (ages 7 and 9 months). The surviving children were 5 months, 1, 1½, 1½, and 5 years of age. Administration as soon as possible of 100,000 units of serum twice in 24 hours, intravenously or intraperitoneally, is recommended. If the bacteria persist in the spinal fluid several days, another 10,000 to 15,000 units should be given. In addition, sulfathiazole and streptomycin should be used.

WALLGREN, Stockholm, Sweden.

HEMOPHILUS INFLUENZAE MENINGITIS TREATED WITH STREPTOMYCIN, SULFONAMIDE, AND TYPE-SPECIFIC RABBIT IMMUNE SERUM. HANS C. ENGBAEK, Ugesk. læger **110**:1355 (Nov. 25) 1948.

Of seven children (ages 4, 7, 11, 13, 14, 24, and 31 months) treated alike with streptomycin, sulfonamide, and type-specific rabbit immune serum, only one died (4 months). All children with Hemophilus influenzae meningitis should be treated with type-specific rabbit immune serum and sulfonamide. In children under 2 years of age streptomycin should also be given, from the start of treatment on; in children above this age streptomycin is recommended only if the effect of serum and sulfonamide within the first 48 hours is not satisfactory.

WALLGREN, Stockholm, Sweden.

SUBACUTE ENCEPHALITIS IN CHILDREN. J. BODDAERT and M. ROLAND, Maandschr. kindergeneesk. **18**:449, 1950-1951.

The clinical history of a case of subacute encephalitis is given. The postmortem examination revealed an inflammatory process especially affecting the white matter. The gray matter was not so seriously involved. The striking features were acute cellular lesions, perivascular infiltrations, and diffuse and nodular glial proliferation. There was no demyelinization. The cerebral cortex, the basal ganglions, the midbrain, and especially the pons and the medulla oblongata were affected. In the cerebellum the most striking changes were found in the dentate nucleus.

FROM THE AUTHORS' SUMMARY.

Psychology and Psychiatry

PSYCHOLOGICAL EDUCATION OF NEWBORN AND CHILDREN. OTAKAR TEYSCHL, Pediat. listy **4**:233, 1949.

The author assumes that the psychological development and the education of newborn and young infants depends on the formation of individually successful conditioned reflexes. This

happens on the basis of the cephalocaudal law of psychosomatic development, which should be considered in the education of infants in order to avoid failure. By clinical observation the author found that the basic congenital reflex of defensive crying localizes itself soon after birth as a conditioned reflex of a lower category; it is used by the newborn infant for purposeful communication with the outer world up to the time that he learns to speak, approximately at the end of one year, when a conditioned reflex of a higher category has been formed. The first social conflict often happens in the newborn period. After learning that crying brings him his mother's attention, the child uses it for tyrannizing his surroundings, and thus he changes from the object which has to be educated into a psychological subject and is on the contrary trying to form a conditioned reflex in his mother (child cries, mother attends). Clinical experience further shows that conditioned reflexes of a higher category (speech, the controlled function of the sphincters, regular nightly sleep) are, as reflexes of a complicated nature and of new development, most vulnerable. Disturbances of the psychological development of infants and small children occur therefore relatively easily, and in the not yet stabilized mechanism such signs as stammering, disturbances of defecation, enuresis, and disturbances of sleep then appear. With the increasing function of the cortex of the brain, it is necessary to start intellectual and moral education. The author divides this education into stimulating and inhibiting processes and outlines the techniques to be used.

FROM THE AUTHOR'S SUMMARY.

SCHIZOPHRENIA IN A GIRL 9 YEARS OLD. K. E. SJÖSTRÖM, Nord. med. **40**:1824 (Oct. 8) 1948.

Sjöström reports a case of schizophrenia in a female patient now 20 years old. The disease developed before the age of 10 years. During the first school year her intellectual attainments were above average. During the second year at school, after an acute febrile disease, probably measles, the condition rapidly deteriorated. In the course of a few months a serious psychosis developed of unmistakable catatonic type. The symptoms included paramimia, delusions, thought disturbances, and autism. After five months of treatment in a mental hospital, she returned to school and completed her school education in a satisfactory manner. She remained, however, mentally abnormal during the whole time. At the age of 17 she again became worse, and now she is in an advanced stage of schizophrenic deterioration of catatonic character.

WALLGREN, Stockholm, Sweden.

FRUSTRATION. H. P. J. KOENEN, Maandschr. kindergeneesk. **19**:277 (Oct.) 1951.

Regulated or sufficiently compensated frustrations are indispensable in the individual and social education of the child.

FROM THE AUTHOR'S SUMMARY.

Diseases of Genitourinary Tract

CONGENITAL LESION OF THE UPPER PORTION OF THE URINARY TRACT. FELIX CANTIN CASTILLO and OSVALDO MONTES R., Rev. chilena pediat. **20**:522 (Dec.) 1949.

The authors report seven clinical histories of congenital malformations of the upper part of the urinary tract. In order to determine the frequency of these congenital malformations, they reviewed 1,509 autopsy reports on children from the files of the Roberto del Rio Hospital. They found 60 malformations of this type, a 4% incidence, and of these, for 18 clinical symptoms were shown; two-thirds of the cases were in boys. The clinical symptoms shown were five bilateral hydronephroses, nine right-sided hydronephroses, and four left-sided hydronephroses. In the other 42 cases the malformations were autopsy findings only and were not manifested clinically.

The authors report on the symptomatology that is produced by the disturbance of the urinary tract: anomaly, obstruction, retention, and infection. Symptoms of pyuria are specially analyzed, as it is frequently found in malnourished infants without a concomitant malformation of the urinary system.

The authors stress the importance of diagnosing the congenital malformations and then proceeding toward a conservative operative treatment, when the condition of the kidney permits. If these conservative procedures do not cure the condition, one can resort as a last chance to nephrectomy.

FROM THE AUTHORS' SUMMARY.

HYPERTENSION AND UNILATERAL KIDNEY PATHOLOGY. O. PAUWELIJN, Acta pædiat. belg. **2**:202, 1948-1949.

The author reports the case of a 7-year-old girl who came to the hospital with complaints of pains in the left loin. The left kidney was enlarged and tender; urinalysis showed red and white blood cells, casts, and increased albumin. There were fever and a blood pressure of 160/100, with vertigo and vomiting. She had presented similar symptoms about 11 months prior to her admission to the hospital. Retrograde pyelography showed hydronephrosis on the left. Urinalysis for the right kidney showed normal results. After the acute infection was cleared with sulfonamides, the left kidney was removed, and the patient made an uneventful recovery. Her latest blood pressure reading was 110/70.

GLASER, Chicago.

SIMPLE METHOD OF ESTIMATING THE INULIN AND PARAAMINO-HIPPURATE CLEARANCES IN NEWBORN INFANTS. JØRGEN VESTERDAL, Acta pædiat. **37**:421, 1949.

A method of determining the inulin and paraaminohippurate clearances in newborn infants is reported. The agents are injected subcutaneously and estimated by a microtechnique in samples of urine obtained by catheter and in capillary blood. The accuracy of the analytical method is, with the concentrations commonly used, about 5% for inulin and 2 to 6.5% for paraaminohippurate.

FROM THE AUTHOR'S SUMMARY.

STUDIES ON THE KIDNEY FUNCTION IN PREMATURE AND FULL-TERM INFANTS BY ESTIMATION OF THE INULIN AND PARAAMINO-HIPPURATE CLEARANCES. JØRGEN VESTERDAL and FOLKE TUDVAD, Acta pædiat. **37**:427, 1949.

Inulin and paraaminohippurate clearances were determined in 55 experiments on infants aged 1 to 118 days with birth weights from 1,100 to 3,750 gm. In the first week of life the inulin and paraaminohippurate clearances were 50 to 60 ml. a minute per 1.73 square meters of body surface. Both increased rapidly in the following weeks, though with great individual variations. There was no significant difference between the values obtained from full-term infants and those obtained from premature infants with birth weights over 1,500 gm. Clearances from infants with lower birth weights were rather low, but not definitely outside the normal ranges. The filtration fraction was on an average 0.32.

Both the inulin and the paraaminohippurate clearances were depressed by pain and, in some of the experiments, increased by increased diuresis. In both cases the filtration fraction remained almost constant, suggesting alterations of the number of active nephrons (by variations mainly in the vasa afferentia).

FROM THE AUTHORS' SUMMARY.

CASE OF OVARIAN AGENESIA. S. VAN CREVELD and O. M. DE VAAL, Acta pædiat. **37**:474, 1949.

Attention is drawn to the syndrome of ovarian agenesia, characterized by disturbance in growth, osteoporosis, and enlarged excretion of gonadotropic substances in the urine; with these symptoms various other ones may be present. Report of a case in a girl 14 years old who was treated with a combined estrogen-androgen therapy is included.

FROM THE AUTHORS' SUMMARY.

Diseases of Ductless Glands; Endocrinology

CLINICAL SURVEY OF VASCULAR COMPLICATIONS IN "JUVENILE DIABETES MELLITUS." HAROLD G. GRAYZEL and HYMAN B. WARSHALL, Pediatrics **8**:506 (Oct.) 1951.

A study of 25 patients with "juvenile" diabetes who had the disease from 11 to 28 years revealed that up to the present time in none of the diabetic patients whose control was considered good did detectable vascular lesions develop. It is not questioned that the incidence of diabetic complications increases with the duration of the disease. However, it is felt that good control will probably postpone the onset of diabetic complications in a significant number of cases and in a similar manner influence the severity of these complications.

FROM THE AUTHORS' SUMMARY.

PRODUCTION OF CONGENITAL DEFECTS IN THE OFFSPRING OF PREGNANT MICE TREATED WITH CORTISONE: PROGRESS REPORT. F. CLARK FRASER and T. D. FAINSTAT, Pediatrics **8**:527 (Oct.) 1951.

It has been shown that cortisone, injected into pregnant female mice, will produce cleft palate and other congenital malformations in the resulting young. The incidence of cleft palate varies according to the genetic constitution of the treated mice, the dosage of cortisone used, and the gestational stage at which treatment is begun. FROM THE AUTHORS' SUMMARY.

HYPERTHYROIDISM IN CHILDREN. KNUD H. OLESEN and E. SCHIÖDT, Ugesk. læger **110**:109 (Jan. 29) 1948.

Seven children (five girls 6 to 10 years of age, two boys aged 11 and 15 years) with hyperthyroidism are reported. The differential diagnosis from rheumatic fever and chorea may be difficult. The disease is usually rather mild in children, and therefore conservative treatment is often effective. Cases of hyperthyroidism without goiter or exophthalmos are not rare in childhood.

WALLGREN, Stockholm, Sweden.

TREATMENT OF THE WATERHOUSE-FRIDERICHSEN SYNDROME. M. G. STRONK, Maandschr. kindergeneesk. **17**:121, 1949.

In the treatment of epidemic cerebrospinal meningitis (Waterhouse-Friderichsen syndrome), shock is most successfully combated by giving an intravenous drip infusion, together with adrenocortical hormone. Sepsis, not always due to meningococci, is best treated by a combination of antibiotics and chemotherapeutic agents. Therapy should commence as soon as possible, as the disease runs a fatal course within 48 hours. A patient treated by the above method recovered within a few weeks.

The clinical syndrome is not always accompanied with hemorrhage in one or both adrenals. It is therefore impossible to consider the adrenal hemorrhage as the cause of shock. As another cause of the accompanying shock, hyperadrenalism or toxemia due to sepsis should be considered. The affect of the administration of adrenocortical hormone would be due primarily to the restored permeability of the capillaries, which secondarily combat shock.

VAN CREVELD, Amsterdam, Netherlands.

THE ADRENOGENITAL SYNDROME. S. J. de JONG, Maandschr. kindergeneesk. **17**:155, 1949.

Symptoms of vomiting and dehydration in a 14-day-old boy were diagnosed as due to hypertrophy of the androgenous zone of the adrenal cortex, after pyloric stenosis was ruled out.

The condition improved by administration of sodium chloride and desoxycorticosterone. The patient was doing well at the age of 2 years, but needed desoxycorticosterone regularly. Slight symptoms of precocious puberty were present.

A second patient, a hermaphrodite, was admitted to the hospital at the age of 16 days because of vomiting and dehydration. This infant also improved rapidly during administration of desoxycorticosterone.

The diagnosis of hyperplasia of the androgenous zone of the adrenals with impairment of the other parts of the cortex was confirmed in both patients by the finding of low sodium and chloride and high potassium levels in the blood. There was an increased excretion in the urine of 17-ketosteroids, especially of those components derived from the adrenal cortex.

VAN CREVELD, Amsterdam, Netherlands.

Diseases of Muscles, Bones, Joints, and Lymph Nodes

SKELETAL DEVELOPMENT IN INFANCY: STANDARDS FOR CLINICAL USE. EARLE L. REYNOLDS and TOSHIKO ASAKAWA, Am. J. Roentgenol. **65**:403 (March) 1951.

Standards for the determination of skeletal development in infants consist of tables which are based on the number of ossification centers present on the roentgenogram of the hand or foot at 10 age levels between birth and 3 years. Development for any particular infant at a certain

age is classified as very fast, fast, average, slow, and very slow, according to the number of ossification centers present.

The authors also present a second table for the determination of the degree of skeletal development based on the presence or absence of other ossification centers not in the hand or foot. These centers are the distal femur, proximal tibia, head of humerus, distal tibia, head of femur, capitellum, greater tubercle of humerus, and distal fibula. The average age at which these centers appear is given, and deficiencies of skeletal development are classified as slow or very slow.

The standard tables were prepared from an analysis of the time of appearance of 63 centers of ossification in 119 normal infants between birth and 3 years. In 1 to 2% of cases there was disagreement in results between evaluation of skeletal development by means of the hand or foot and assessment of skeletal development by means of the skeleton as a whole.

HODGSON, Rochester, Minn.

DIAGNOSTIC CONTRIBUTIONS OF THE ELECTROMYOGRAM. JAMES G. GOLSETH, California Med. **73**:355 (Oct.) 1950.

When muscles contract, they generate electricity. This muscle electricity can be seen and heard on the electromyograph. Normal muscles generate a different type of electrical impulse than do paralyzed muscle, and for this reason the electromyograph is of great assistance in the diagnosis, prognosis, and treatment of such conditions as poliomyelitis, nerve injuries, and strokes.

PRYOR, Redwood City, Calif.

THE STRONTIUM CONTENT OF HUMAN BONES. ROBERT M. HODGES, NORMAN S. MCDONALD, RALPH NUSBAUM, RICHARD STERNS, FLORITA EZMIRLIAN, PATRICIA SPAIN, and CLARE MCARTHUR, J. Biol. Chem. **185**:519 (Aug.) 1950.

Spectrographic analyses for strontium were made on samples of bone ash from 26 persons varying in age from the fetus to 75 years. The strontium content of all the fetal specimens lay in the range of 0.015 to 0.019% (average 0.016%). The range for all the other specimens was from 0.16 to 0.44%, with an average value of 0.24%. These values, which are expressed in terms of percentage of strontium in the bone ash, are seen to remain constant during the life span except for during the fetal life. Within any given person there were no significant differences in strontium content between parietal, vertebral, rib, or femur bone. The strontium content of the bones of 12 persons who died shortly prior to 1914 was not significantly different from that found in the 1949 series.

FORBES, Dallas, Texas.

DYSTROPHIA MYOTONICA AND MYOTONIA CONGENITA: HISTOPATHOLOGIC STUDIES WITH SPECIAL REFERENCE TO CHANGES IN THE MUSCLES. G. WOHLFART, J. Neuropath. & Exper. Neurol. **10**:109 (April) 1951.

Wohlfart reports studies made in 19 cases of dystrophia myotonica and five cases of myotonia congenita. Autopsy was performed in one case of dystrophia myotonica in which the spinal cord, sympathetic chain, peripheral nerves, and muscles were investigated histopathologically. Muscle biopsies were done in the other cases.

In the case of dystrophia myotonica with autopsy no histopathologic changes were observed in the spinal cord, the sympathetic chain, or the peripheral nerves. Fiber analysis by a special method revealed no pathologic change in the ventral or dorsal spinal roots.

Microscopic changes in the muscles were found to be, under certain conditions, pathognomonic of the disease in question. Wohlfart calls attention to the following points: 1. The only constant histopathologic change in dystrophia myotonica is an inward migration of nuclei from the periphery of the muscle fibers to the center, where they divide and form long chains. The migrating cells lose their immediate contact with the capillaries. Capillary loops and surrounding tissues are inclined to grow into the muscle fibers toward the nuclear rows. 2. In dystrophia myotonica the myofibrils are often destroyed without a corresponding decrease in the sarcoplasm content. 3. The striated fibrillar rings (striated annulets, the *Ringbinden* of Heidenhain, which were described by him as specific for myotonia) are rather common in dystrophia myotonica.

However, they are also to be found in many muscles of advanced age and, especially, in the extrinsic muscles of the eye, as well as in muscular atrophy from disease and in progressive muscular dystrophy. 4. The histopathologic changes in myotonica congenita consist mainly of general hypertrophy of the muscle fibers and slight alterations which are reminiscent of the changes encountered in the early stages of dystrophia myotonica.

ALPERS, Philadelphia [A. M. A. ARCH. NEUROL. & PSYCHIAT.].

INFLUENCE OF HEREDITY ON THE PNEUMATIZATION OF THE TEMPORAL BONE. HUGH W. SCHWARTZ, J. Laryng. & Otol. **65**:317 (May) 1951.

There is much confusion about pneumatization of the temporal bone and as to whether there is more than one normal type. Wittmaack stated that at birth the tympanic cavity, attic, and antrum are filled with a myxomatous tissue covered with cuboidal epithelium; during the first year the subepithelial tissue is absorbed, and the epithelium lines these cavities. This epithelial-covered myxomatous tissue grows into the marrow spaces of the temporal bone, where the same process occurs, forming the mastoid air cells. He held that interference with this process by entrance of amniotic fluid, meconium, or other substances into the middle ear or by infantile otitis media arrests the pneumatization and results in diploic or sclerotic mastoids.

Smith agreed with most of these views but felt that the constitution of the osseus tissue, rather than infection, arrested development. Schwartz felt that the inherited quality of the myxomatous tissue determined the type of mastoid. Many facts are presented to throw doubt on these theories. It has been stated that over 90% of newborn infants have otitis media neonatorum. Roentgenograms of children who have had otitis media in infancy often show pneumatized temporal bones. In patients with acute mastoiditis who had no surgical treatment, pneumatized mastoids have later developed. Chronic disease in a pneumatized bone produces a fibrotic rather then a sclerotic mastoid. .

Schwartz feels that heredity is the main factor influencing the type of temporal bones that will develop and adequately supports this idea by finding the same type of pneumatization in 19 sets of 25 sets of identical twins and by large-scale roentgenographic studies of family groups, which show a strong tendency for members of the same family to have the same type of temporal bone pneumatization.

LEJEUNE and LEURS, New Orleans [A. M. A. ARCH. OTOLARYNG.].

THE GENERALIZED DEVELOPMENTAL OSSEUS DYSTROPHIES: 8. OSTEO-DENTAL DYSPLASIA (CLEIDO-CRANIAL DYSOSTOSIS): GENERAL SUMMARY. W. P. U. JACKSON, South African M. J. **25**:475 (July 7) 1951.

The syndrome of cleidocranial dysostosis is briefly discussed. This is the final article in a series of eight in which the author has attempted to present simply some of the developmental bony dystrophies and to show that the different syndromes are clearly defined and fit into simple classification.

McGUIGAN, Evanston, Ill.

STILL'S DISEASE. I. WALT, J. D. RAFTERY, and P. A. JOHNSON, South African M. J. **25**:541 (Aug. 4) 1951.

A 10-year-old girl with multiple rheumatoid arthritis (Still's disease) was treated with cortisone over a period of three months. Response was prompt and effective, but relapses occurred. An intermittent improvement was maintained, but pericarditis developed nevertheless.

McGUIGAN, Evanston, Ill.

EXPERIENCES IN THE TREATMENT OF JUVENILE RHEUMATOID ARTHRITIS WITH ACTH. S. VAN CREVELD, E. DINGEMANSE, L. G. HUIS IN'T VELD, and F. KUIPERS, Ann. pædiat. **176**:201 (April) 1951.

The clinical, biochemical, and hormonological data obtained in three children suffering from juvenile rheumatoid arthritis and treated with corticotropin (ACTH) for six, four, and three months, respectively, are presented. Division of the total amount given into four injections

daily caused a stronger effect on the excretion of 17-ketosteroids and made it possible to gain a clinical improvement by giving a very small total dosage. Signs of intoxication which necessitated discontinuance of therapy occurred in one case. These symptoms have improved since. One other patient became refractory to the drug after five months. A striking improvement was gained in all patients compared with the condition before treatment. The determination of the antihyaluronidase titers did not help in evaluating the clinical activity of the rheumatic process.

FROM THE AUTHORS' SUMMARY.

FAMILIAL DISTURBANCE OF THE SKELETON WITH MULTILOCULAR ASEPTIC BONE NECROSIS ESPECIALLY WITH OSTEOCHONDRITIS DISSECANS. H. ZELLWEGER and M. EBNOTHER, Helvet. pædiat. acta **6**:95 (April) 1951.

A description is given of several cases of multiple epiphyseal and metaphyseal lesions of dominant heredity occurring in one family. The bone lesions lead to multilocular aseptic necroses of the bones and to early appearance of arthrosis deformans. All four cases present nanism. Two male members of the family have signs of hypogenitalism, one of them with nycturia and a lowered blood sugar level, the other one with an increased basal metabolism. Both boys show behavior problems.

FROM THE AUTHORS' SUMMARY.

TENDOVAGINITIS STENOSANS, A TYPICAL AFFECTION OF CHILDHOOD. M. GROB and M. STOCKMANN, Helvet. pædiat. acta **6**:112 (April) 1951.

The authors describe an affection called tendovaginitis stenosans about which, until recently, little has been known. It is of relatively frequent occurrence and is typical for early childhood. Observation of 39 cases has shown the following signs to be characteristic: Extension of the terminal phalanx of the fingers, especially of the thumb, is hindered owing to a disproportion of the flexor tendon and its sheath at the level of the metacarpophalangeal joint. The affection is caused by an abnormal development of the sesamoid bones, and the histologic findings point to a pure mechanical causation. Dissection of the tendon sheath gives always good results.

FROM THE AUTHORS' SUMMARY.

TWO CASES OF EARLY MALIGNANT OSTEOPETROSIS (ALBERS-SCHÖNBERG DISEASE). A. GIAMPALMO and P. TOLENTINO, Minerva Pediat. **1**:447 (Dec.) 1949.

Two cases of rapidly fatal osteopetrosis, one in a 20-day-old girl and the other in a 3-month-old girl, are reported with autopsy findings. The clinical picture was of poor nutrition, splenomegaly, anemia, thrombopenia, and rhinitis. Roentgenograms revealed the typical marble bones. The explanation given for the osteopetrosis is insufficient osteoclastic and abnormal osteoplastic activities; there is metaplasia of the cartilaginous cells, which fill up the medullar cavities to displace bone marrow tissue.

HIGGINS, Boston.

AXIAL DYSPLASIA OF THE FIFTH LUMBAR VERTEBRA. P. GRAZIADEI, Pediatria **57**:918 (Nov.) 1949.

Of 132 children examined, aged 5 months to 12 years, the fifth lumbar vertebra was found to be tilted in 57 (43%). This abnormality may frequently lead to scoliosis.

HIGGINS, Boston.

DIAGNOSTIC, THERAPEUTIC, AND SOCIAL PROBLEMS OF CONGENITAL LUXATION OF THE HIP. JOSÉ MAESTRE HERRERA, Acta pediat. españ. **83**:1321 (Nov.) 1949.

For the diagnosis of congenital luxation of the hip, a detailed, careful history should be obtained, including such things as (1) consanguinity, (2) congenital anomalies, and (3) type of birth, especially as regards forceps delivery and podalic presentations. The history of all injuries and illnesses of the mother during pregnancy should be included.

The mother may note a crepitation in the hip joint or pain on handling, especially when changing the child's diaper. There may be crepitant sensations in the joint when it is moved

successively in abduction, flexion, and extension, owing to the movement of the head of the femur against the posterior border of the cartilages surrounding the joint. Since this is found in a certain number of normal babies, it should be considered only confirmatory evidence.

The author discusses the roentgen diagnosis by use of flat roentgenograms and the use of contrast media, air, or an opaque dye. Many arthrograms showing normal and abnormal hips are included in the article. The author has never seen any deleterious results from use of contrast media in joints.

Differential diagnosis must be made between this condition and (1) coxa vara, (2) obstetrical dislocation, (3) true inequality of extremities, (4) paralytic hip of Verneuid, (5) suppurative arthritis, and (6) any lesions of the epiphysis.

Manipulation is better than surgery and consists of (1) reduction and (2) immobilization in plaster. This is done with use of anesthesia and with the patient on the "quilted pedestal of Putti." Care must be taken so that soft tissues are not injured. During manipulation the following accidents may occur: (1) fracture of the femur, (2) nerve injury, especially to the sciatic nerve, (3) hematomas, and (4) sudden death from shock. In cases in which surgery is absolutely necessary, the author recommends the technique used by Levent.

In a discussion of the social problems involved, the author says that education and proper facilities are essential, but economic and psychic improvement of these patients would more than outweigh expenses such as those for proper clinics, teachers, and materials.

ALLEN, Santa Fe, N. M.

CARDIOARTICULAR RHEUMATISM IN INFANCY. JAMIL JOAQUIM, Arq. pediat. **23**:43 (Dec.) 1950.

The author gives a discussion of rheumatic fever and mentions the need for an organized plan of prevention and treatment.

CHRISTOPHERSON, Evanston, Ill.

ARTHROGRAPHY IN DISLOCATION OF THE HIP. ARMANDO DOBERTI B., Rev. chilena pediat. **22**:1 (Jan.) 1951.

A simple roentgenogram is not sufficient for the diagnosis of congenital dislocation of the hip. An arthrographic study should always be done. This procedure is easy and harmless and establishes the prognosis and indicates the proper treatment. It also aids in the differential diagnosis as well as controls the technique of reduction. Arthroplanigraphy is a very useful aid, especially in the diagnosis of tumors of the acetabulum.

FROM THE AUTHOR'S SUMMARY.

X-RAY STUDIES OF BONE MARROW INFUSION WITH CONTRAST MEDIA. HEINZ SPIESS, Monatsschr. Kinderheilk. **98**:217 (May) 1950.

It was demonstrated by roentgenograms that radiopaque contrast medium infused by sternal and tibial marrow routes flowed directly into veins, thus equaling in effect an intravenous infusion. Local bone lesions were seen in all cases, and slowness of bone marow infusion is advisable to minimize osteomyelitis.

HARTENSTEIN, Madison, Wis.

NORMAL VALUES AND VARIATIONS IN THE DEVELOPMENT OF THE CARPAL CENTERS. F. SCHMID, Ztschr. Kinderh. **65**:646, 1948.

Length and width measurements of the carpal centers as well as the dates of appearance were studied on several hundred roentgenograms of children from birth to puberty, and the findings are recorded in table form and graphically. Neither sex nor constitutional variations seem to influence the data gathered from normal subjects. Asymmetries of development point toward a pathological process. Although comparison with earlier data of investigators was difficult, because of the variations in methods, a slight acceleration of the appearance of ossification centers was noted.

GLASER, Chicago.

PAINFUL PRONATION. JOSEF PROCHAZKA, Pediat. listy **4**:249, 1949.

On the basis of his autposy studies and studies of 102 patients with painful pronation treated at the orthopedic clinic, the author comes to the conclusion that painful incomplete dislocation

(subluxation) of the head of radius among children is caused aside from other circumstances, such as a shorter radius in childhood, mainly by higher elasticity of the upper end and head of the radius. Data on this elasticity are given by age, and it disappears with advancing ossification, vanishing completely at the fifth year of age, i. e., with the appearance of the ossification center for the capitulum radii. The subluxation itself is caused in the main by an overexaggerated pronation of the forearm when the elbow is extended, whereby the head of the radius is forcibly extracted from the annular ligament and is fixed in this position by an interposed fold of the hinder part of the joint capsule between the capitulum radii and the eminentia capitata humeri.

FROM THE AUTHOR'S SUMMARY.

DYSOSTOSIS ENCHONDRALIS EPIPHYSARIA (RIBBING). LUBOMIR PELIKAN, Pediat. listy **5**:273, 1950.

A description is given of the condition occurring in two siblings (a boy of 9 years and a girl of 7 years). The other three siblings are healthy.

FROM THE AUTHOR'S SUMMARY.

SEVERE MYOCARDIAL DAMAGE IN CHRONIC ATROPHIC ARTHRITIS. HANS-OLOF MOSSBERG, Acta pædiat. **37**:485, 1949.

Chronic atrophic arthritis and acute rheumatic infection commonly show clinical pictures clearly divergent with regard to symptomatology and course. A case is described in which the clinical symptoms at the onset were in closer agreement with the acute form but in which there gradually developed chronic atrophic arthritis with uncommonly marked myocardial changes.

FROM THE AUTHOR'S SUMMARY.

MYASTHENIA GRAVIS OF A NEWBORN CHILD. IVAR NILSBY, Acta pædiat. **37**:489, 1949.

A case of a newborn child with myasthenia gravis whose mother also had myasthenia gravis is described. One similar case has been found in the literature. After five weeks the symptoms disappeared. The theory is advanced that a substance which causes the mother's disease is transmitted during intrauterine life to the child, producing the picture of myasthenia gravis. It takes several weeks after birth for the child to free itself of this substance, whereupon the symptoms of myasthenia gravis disappear. The importance of extremely careful hospital treatment during the first weeks is emphasized.

FROM THE AUTHOR'S SUMMARY.

CONGENITAL CHONDRODYSTROPHIA CALCIFICANS IN ASSOCIATION WITH OTHER ABNORMALITIES. CORNELIA DE LANGE and TIELINE JANSSEN, Maandschr. kindergeneesk. **17**:67, 1949.

The child reported was born at full term, was asphyctic, and had short upper arms, a short neck, and a folded skin. Roentgenograms showed calcifications in the region of the patella, the trochanters, around the hip joints and the distal parts of the ischia and the calcanus tubes. At the age of 5 weeks jaundice developed with symptoms of bile stasis. The liver was not enlarged. The urine contained bilirubin, and the direct van den Bergh reaction was positive (26 units). The child did not gain weight. At the age of 8 weeks the temperature rose and hemorrhagic diathesis developed, and the infant died a few days later. Autopsy revealed a paucity of intrahepatic bile ducts, embryonic tubules, and cyst formation in the kidneys.

VAN CREVELD, Amsterdam, Netherlands.

RHEUMATOID ARTHRITIS IN YOUNG CHILDREN TREATED WITH GOLD. R. K. W. KUIPERS and M. F. SCHOUTEN, Nederl. tijdschr. geneesk. **93**:4235 (Dec. 17) 1949.

Nineteen children suffering from rheumatoid arthritis were treated with gold (aurothioglucose [solganal®]). Treatment was started at an average age of 7 years. Some patients could be followed seven years after the first course was completed, and some relapses were noted. A new course with gold salts, however, brought a favorable result again. The authors consider their results as "good" in 12, "moderate" in 4, and "bad" in 3 patients. Two of these died. The clinical history of three patients is reported in some detail.

The initial dose was 5 mg. and this was slowly increased to 50 or 80 mg. according to age and body weight. Physical therapy is an important aid in reconditioning the children. Kuipers and Schouten's experiences are at variance with those of Schlesinger and are more optimistic.

VAN CREVELD, Amsterdam, Netherlands.

Diseases of Eye

RETROLENTAL FIBROPLASIA. P. M. MOFFATT, Proc. Roy. Soc. Med. **43**:223 (March) 1950.

Previous to December, 1949, no paper had appeared in Britain under the title of retrolental fibroplasia. Previous to this time, all the references were to be found in American journals. Since Terry's original report in 1942, there has been a large volume of literature on the subject. The author reviews the findings and reports of Terry, Owens, Gilger, and others. The pathology and probable causative factors are briefly discussed. Operative treatment, through (1) needling and (2) removing of the opaque tissue by a posterior route, has been unsatisfactory. A brief discussion of the pathology of this condition is presented by Mr. Eugene Wolff, with several case reports by others.

HEARD, Monterey, Calif.

Cutaneous Diseases; Allergy

ATOPIC DERMATITIS—ETIOLOGY AND CLINICAL MANAGEMENT. LOUIS TUFT, California Med. **73**:233 (Sept.) 1950.

Atopic dermatitis is primarily an allergic problem, similar in most of its aspects to that of allergic bronchial asthma. It should be studied and treated like asthma, with especial emphasis on the significance of inhalant allergens. It is doubtful that psychic factors are of importance in primary genesis of the disease, although they may be involved in exacerbation of it.

PRYOR, Redwood City, Calif.

LOCAL NASAL THERAPY WITH PYRIBENZAMINE IN SEASONAL AND NONSEASONAL HAY FEVER. EMANUEL SCHWARTZ and HARRY LEIBOWITZ, J. Allergy **20**:269 (July) 1949.

A 0.5% isotonic buffered solution of tripelennamine (pyribenzamine®) hydrochloride gives relief when applied to nasal mucous membrane. It can be applied as drops or as spray for relief of seasonal and nonseasonal hay fever.

HOYER, Cincinnati.

EFFECT OF X-RAY RADIATION ON HYPERSENSITIVENESS. LEO H. CRIEP, LLOYD D. MAYER, and SHELDON G. COHEN, J. Allergy **21**:373 (Sept.) 1950.

Study was made of the effect of x-ray radiation on the development of vascular disease, the Arthus phenomenon, the Schultz-Dale reaction, and the production of precipitins in sensitized animals. Forty adult rabbits were used; 22 were irradiated before sensitization, 4 were irradiated without sensitization, and 8 were sensitized but were not irradiated.

In the group that was irradiated and later sensitized, there was marked reduction in the number and intensity of vascular lesions; the Arthus phenomenon was negative, and the precipitin reactions were depressed. The Schultz-Dale reactions were inconclusive. There was marked leucopenia and depression of lymphocyte counts in the irradiated animals as compared with the controls.

"X-ray radiation of normal non-sensitized animals showed no lesions of diffuse vascular disease or carditis."

HOYER, Cincinnati.

SOME PRACTICAL ASPECTS OF ALLERGY. SUSAN C. DEES, J. Pediat. **37**:685 (Nov.) 1950.

The author's discussion ranges from immunology to pharmacology, from pollens to recipes, from psychosomatics to house furnishings. Through it all runs her theme: The pediatrician can take care of most allergic problems in his patients if he will acquire a little more information about the common allergens and if he will remember that allergic diseases vary in intensity.

MACDONALD, Pittsburgh.

AMMONIA DERMATITIS: TREATMENT WITH DIAPERENE CHLORIDE OINTMENT. MEYER L. NIEDELMAN and ADOLPH BLEIER, J. Pediat. **37**:762 (Nov.) 1950.

Diaperene chloride® (p-di-isobutyl-cresoxy-ethoxy-ethyl-di-methyl benzyl ammonium chloride monohydrate) ointment was applied to the diaper area of 107 infants with ammoniacal dermatitis. All but 8 had rapid clearance. Three of the failures may have been due to an atopic dermatitis with secondary infection. It appears from patch tests that the ointment has no sensitizing properties.

MACDONALD, Pittsburgh.

THE TREATMENT OF SCABIES IN AN INSTITUTION: COMPARATIVE STUDY. BERNARD APPEL, New England J. Med. **243**:74 (July 20) 1950.

Three modern scabetics were used on 328 patients in three separate wards of a state mental institution: 0.5% gamma isomer of benzene hexachloride in a vanishing cream base (kwell® ointment), benzylbenzoate, and 10% N-ethyl-O-crotonotoluide (eurax®). All patients were clinically free of the infestation at the end of the treatment period. No untoward results of the treatment were observed, and the conclusions drawn indicate that the modern agents are superior to the formerly popular sulfur preparations.

WHEELOCK, Denver.

INTRACRANIAL COMPLICATIONS OF CONGENITAL DERMAL SINUSES. DONALD D. MATSEN and FRANC D. INGRAHAM, Pediatrics **8**:463 (Oct.) 1951.

When the cleavage of neural ectoderm from epithelial ectoderm is incomplete, a persistent cutaneous sinus may extend anywhere from the deeper layers of the skin into the central canal of the brain or spinal cord. These have been described frequently as occurring in the lumbosacral region but not intracranially. Ten cases are described in which intracranial extension of a congenital dermal sinus was disclosed at operation.

The complications of this lesion include infection in the form of meningitis, abscess formation, and osteomyelitis, as well as hydrocephalus due to obstruction of the spinal fluid pathways. In unexplained meningitis the entire midline area of skin over the neural axis should be examined carefully for evidence of a dermal sinus opening. Whenever a dimple or subcutaneous mass is found in the midline of the scalp, roentgenograms should be examined carefully for an underlying skull defect. When such a defect exists, intracranial exploration is indicated. Surgical treatment previous to development of intracranial infection is relatively simple and should be rewarded by complete cure. Excision after infection has occurred is difficult and the results in the group reported have been poor.

FROM THE AUTHORS' SUMMARY.

ANTIALLERGIC PROPERTY OF VITAMIN B_6. ARRICO GALEOTTI FLORI and LEONARDO DONATELLI, Riv. clin. pediat. **47**:401 (June) 1949.

Experimental research which showed the antiallergic action of vitamin B_6 is reported by Flori and Donatelli.

FROM THE AUTHORS' SUMMARY.

GANGRENOUS DERMATITIS IN THE INFANT. JORGE ROSSELOT and RODOLFO BURDACH, Rev. chilena pediat. **51**:200 (May) 1950.

The authors report the clinical history of a 15-month-old infant that presented clinical and histological lesions of dermatitis gangrenosa infantum. Both Pseudomonas aeruginosa and hemolytic Staphylococcus were supposed to have played an etiologic role.

FROM THE AUTHORS' SUMMARY.

Society Transactions

SOCIETY FOR PEDIATRIC RESEARCH

Harry H. Gordon, M.D., *President*

Twenty-First Annual Meeting, Atlantic City, N. J., May 2 and 3, 1951

Third Session

Thursday Morning, May 3

Citrovorum Factor and Aureomycin in Experimental Folic Acid Deficiencies. Dr. Harry A. Waisman, Dr. Joaquin Cravioto-Munoz (by invitation), Dr. Morris Green (by invitation), and Dr. J. B. Richmond, Chicago.

A comparison of the folic acid deficiencies produced either by using a folic acid antagonist, 4-aminopteroylglutamic acid ("aminopterin"), or by using a diet containing 2% phthalylsulfathiazole (sulfathalidine®) has provided evidence that the deficiencies are not identical in all respects. Twenty-four-day-old white rats given 100 γ of 4-aminopteroylglutamic acid per 100 gm. of diet do not grow optimally and begin to show a weight plateau and finally fail after four weeks on the diet. Blood studies revealed that the antagonist also depressed the white cell count and erythropoietic function of the bone marrow. The administration of 1 to 5 mg. of folic acid per 100 gm. of diet counteracted the effect of the antagonist. A single injection of 0.75 mg. of citrovorum factor given to rats that were failing on the 4-aminopteroylglutamic acid diet caused a marked growth response together with a correction of the leukopenia. It was found that citrovorum factor was between 10 and 20 times as active as folic acid in correcting the antagonist-induced deficiency.

The folic acid deficiency produced in four to six weeks by the inclusion of 2% phthalylsulfathiazole in the diet was characterized by a weight plateau, depression of all white cell elements, unkempt fur, and diarrhea. The administration of 5 mg. of folic acid per 100 gm. of diet to these rats resulted in a correction of the deficiency. Citrovorum factor was also effective at levels of 0.75 mg.

It was found that crystalline aureomycin at 5 or 10 mg. per 100 gm. of diet was completely able to overcome the toxic effects of the folic acid antagonists but was ineffective in counteracting the deficiency produced by the phthalylsulfathiazole diet. It was found further that destroying the antibiotic activity of aureomycin by heat or by maintaining it at room temperature in solution for a period of 60 days also made it unable to counteract the effect of the antagonist. It is of interest that other antibiotics, such as penicillin, chloramphenicol (chloromycetin®), terramycin, and streptomycin, did not give the effect that aureomycin did. At the present time further work is being done to elucidate the mechanism of both types of folic acid deficiencies.

Folic Acid and the Synthesis of Pentose Nucleic Acids: A Study of the Liver Cells of Megaloblastic Monkeys Using Chemical Methods and Incorporation of Radioactive Phosphorus. Dr. Charles Upton Lowe, Cyrus P. Barnum, Ph.D. (by invitation), and Dr. Charles Davidson May, Minneapolis.

With a megaloblastic bone marrow as the criterion of a deficiency of pteroylglutamic acid, it has been possible to study the effect of pteroylglutamic acid upon the rate of synthesis of pentose nucleic acid in the liver of monkeys. For the purposes of this report, the amount of pentose nucleic acid, desoxypentose nucleic acid, and the rate of incorporation of P^{32} into various nucleic acid fractions were determined. Preliminary to the chemical and physical determinations, the livers were fractionated into four cytoplasmic and three nuclear components. The present study concerns particularly the total desoxypentose nucleic acid and pentose nucleic acid and the nuclear pentose nucleic acid.

Since in the process of rendering the monkeys megaloblastic, they were also made scorbutic, and frequently refused to feed well, control animals included the following: (1) well-fed normal

monkeys, (2) animals scorbutic but not deficient in pteroylglutamic acid, and (3) starved animals not deficient in pteroylglutamic acid. Also studied were (4) megaloblastic animals and (5) megaloblastic animals to which 15 mg. of pteroylglutamic acid had been given 13 hours before they were killed. P^{32} was administered after a 22-hour fast, one hour before the animals' livers were removed for study.

Calculations were made, based upon the fact that the desoxypentose nucleic acid concentration in each nucleus in a nonproliferating organ such as the liver is constant. The values obtained were expressed as percentage of normal. The following average observations were made:

1. Inanition reduced the pentose nucleic acid/desoxypentose nucleic acid ratio of the whole cell by 25%. Scurvy had little effect upon this ratio. Megaloblastosis caused a decrease of 21%. The administration of pteroylglutamic acid caused an increase to above normal. The percentage of increase between the megaloblastic and the treated animals was 132.

2. In the studies of the isolated nuclear pentose nucleic acid, the changes in the pentose nucleic acid/desoxypentose nucleic acid ratios were of the same order of magnitude as the whole cell changes, with the exception of the increase in the animals treated with pteroylglutamic acid. Here the increase after pteroylglutamic acid administration was 187%.

3. The nuclear pentose nucleic acid of each unit of desoxypentose nucleic acid was multiplied by the activity of the pentose nucleic acid itself (the activity being expressed as percentage of the inorganic phosphorus activity). This yielded an expression which was related not only to the amount of pentose nucleic acid present, but also to its rate of incorporation of P^{32}. This average when related to the normal value, was —22% for the starved animals, +13% for the scorbutic animals, —42% for the megaloblastic animals, and +22% for the megaloblastic animals given pteroylglutamic acid. The percentage of increase of this last group over the untreated megaloblastic animals was + 212.

These data can be used to support the thesis that at least a part of the altered biochemistry of megaloblastic animals is decreased ability to synthesize pentose nucleic acid. It is obvious that in the bone marrow, a rapidly proliferating tissue, this disability may be of more serious consequence than in a resting organ such as the liver.

DISCUSSION

DR. CHARLES D. MAY, Minneapolis: One wonders whether Dr. Waisman's experiments had any application to the use of 4-aminopteroylglutamic acid in the treatment of leukemia. Does he feel that giving aureomycin to patients with leukemia being treated with 4-aminopteroylglutamic acid might tend to neutralize the effects of the acid?

It is important to realize that there may be difficulties in the behavior of the various species so far as the effects of aureomycin on the intestinal flora or the elaboration of citrovorum factor is concerned. In our experiments with monkeys in which megaloblastic anemia has developed, we have found that large amounts of aureomycin have no effect on the megaloblastic marrow. This would indicate that in a monkey on a milk diet the intestinal flora is not of such character that aureomycin will permit the elaboration of citrovorum factor in sufficient quantities to influence the megaloblastic marrow under the conditions of the experiment. Thus, it is obvious that caution must be exercised in applying the results of Dr. Waisman's experiments directly to another species consuming this diet and probably having a different type of intestinal flora.

DR. CALVIN WOODRUFF, Nashville, Tenn.: I think that Dr. Lowe and Dr. May should be complimented on a beautiful piece of work. It approaches the problem of how both folic acid and citrovorum factor may work in the clinical folic acid deficiency in megaloblastic anemia, if it is really folic acid deficiency, which fact has not been exactly proved.

In commenting on Dr. Waisman's paper, I should like to point out that he has given most of his supplements by mouth and that there are two very complicated problems involved: these are the relationship of these various vitamins and antibiotics and other growth factors which are not too well recognized to the intestinal flora as well as to the host organism, and the fact that it is sometimes very difficult to conclude exactly where this action lies. So far as our clinical problem is concerned in working out the pathogenesis of megaloblastic anemia in infancy, we know practically nothing about the growth of the microflora, and we are a little at a loss to

know what part is played by synthesis of these vitamins in the intestinal tract, the role of various growth factors and growth inhibitors on these organisms, and their eventual effect on the whole animal.

Dr. Wolf W. Zuelzer, Detroit: I should like to join with Dr. Woodruff in expressing my admiration for the work that has been presented here. Although some of the ultimate questions still remain to be settled, this work has carried us a long way in the understanding of the deficiency syndromes in question.

In a very small way, I might offer some clinical information on megaloblastic anemia. The fact is, as Dr. May has intimated, that megaloblastic anemia has become a rare condition, and consequently it is very hard to put our theories to the test in the human disease.

We have had the opportunity to try both aureomycin and citrovorum factor on infants with megaloblastic anemia, and, so far as we are able to tell, aureomycin does not have the effect of transforming the bone marrow from a megaloblastic into a normoblastic pattern. That goes along with what Dr. May just mentioned having observed in the monkey.

The citrovorum factor, on the other hand, in our experience has produced a very clear-cut effect on megaloblastic anemia in infants and probably quantitatively far surpasses that of folic acid, with the result that the animal experiment seems to be borne out by the experiments in humans.

Dr. Harry A. Waisman, Chicago: I am grateful to the discussants for their comments. I should say, in regard to Dr. May's question, that the natural consequence of our work will, of course, indicate that if one gives 4-aminopteroylglutamic acid to children with severe leukopenia, one should not give the antibiotics simultaneously. However, on the basis of this study of children with acute leukemia who had received antibiotics, I am not convinced that aureomycin is an antiantagonist of 4-aminopteroylglutamic acid; the concurrent administration of aureomycin, then, would not nullify the beneficial effects of 4-aminopteroylglutamic acid. In other words, there seems to be a dissociation between the animal work and that observed in the patients.

The fecal excretion study which Dr. May mentioned has been done in many animal experiments by other workers, and it has actually been noted by Nichol and Welch, at Western Reserve University, that if one simply provides folic acid, the amount of citrovorum factor which is excreted in the intestine is very high, but even more important, the folic acid content of the liver very markedly increases the citrovorum content, which is, of course, compatible with the idea that as one progresses along the course of coenzyme pathways essential for the ultimate formation of desoxyribonucleic acids, one would obtain the beneficial effects even more efficiently with citrovorum factor than one would obtain it with folic acid.

Dr. May touched on a very important point which we, of course, are aware of, and that is the intestinal flora of the species with which we are dealing. For the last few days in Cleveland, at the Federation of American Societies for Experimental Biology meetings, much time was spent in contrasting the effects of the antibiotics on the flora of poultry, of large and small farm animals, and, of rats and bacteria, and it is very interesting that one finds these differences which are dependent largely on the inherent flora in these animals, which is, of course, a reflection again of their particular type of feed.

Dr. Woodruff pointed out that all of our material was given by mouth. You will remember that I said that aureomycin was given intraperitoneally or was given by mouth and both were equally effective in overcoming the folic acid deficiency induced by 4-aminopteroylglutamic acid. This, of course, opens up the large question which has been extant in the nutritional literature for some time on the role of intestinal synthesis in providing various growth factors to the host animal. It is not an insignificant consideration when one remembers that the bacterial flora changes with age and is different in the breast-fed, the formula-fed, and the diversely fed infant; of course, the fact that our injections of aureomycin were effective does not completely deny the role of intestinal synthesis, because it has been shown that intraperitoneally injected aureomycin is reexcreted into the intestinal tract, and its antibiotic effect can be noted in the lower bowel.

It is very interesting that Dr. Zuelzer did not find any effect of aureomycin on the megaloblastic anemias. I think, again, it is a matter of quantity. One may not completely get all the citrovorum factor which one needs for the correction of the megaloblastic anemia, in spite of the fact that it is much more efficient on a quantitative basis than is folic acid. It would not be

at all surprising, on the basis of the structural formula and the activity of relative coenzymes, that citrovorum factor is much more effective than folic acid in treating megaloblastic anemia.

I think I should comment on Dr. Lowe's paper in that, when we were doing early work on these rats, we found no effect whatever with use of 50 to 100 mg. of ascorbic acid in our folic acid deficiencies. Just yesterday a paper was reported in Cleveland, by Dr. Daft of the National Institutes of Health, which indicated that in several anemias, induced in a variety of ways, including very high amounts of ferric salts, if one gave 2% of the diet of ascorbic acid one got improvement in the anemia.

DR. CHARLES UPTON LOWE, Minneapolis: The discussants have been most kind in their comments.

There are two points which perhaps need clarification. I hope that we have not been understood to say that the only defect in megaloblastic anemia of monkeys (that is, in this particular type) is an inability to synthesize the pentose nucleic acids. Apparently there is such a defect, but other defects may exist, the most obvious of which would be present in a rapidly proliferating organ such as the marrow, and that is an inability to synthesize the desoxypentose nucleic acids. But remember we were concerned with a nonproliferating organ, the liver, whose need for new desoxypentose nucleic acid is slight.

The other point concerns vitamin C. I do not think it would be proper to compare the rat that is deficient in folic acid with the monkey that is deficient in folic acid, since the rat normally is presumed to be able to synthesize his own vitamin C, and monkeys are not able to do so.

Sulfobromophthalein (Bromosulphalein®) Sodium Dye Excretion Test. DR. WILLIAM OBRINSKY (by invitation), DR. MALCOLM L. DENLEY (by invitation), and RALPH W. BRAUER, PH.D. (by invitation), New Orleans.

To evaluate the extent and duration of hepatic immaturity of the premature infant, 35 healthy premature infants of varying chronologic age and weight were subjected to the sulfobromophthalein (bromsulphalein®) sodium dye excretion test. Five milligrams per kilogram was injected intravenously, and serial blood samples were drawn at 3, 8, 15, 30, 45, and 60 minutes. In some patients additional specimens were obtained at 2, 4, and 18 hours. Sulfobromophthalein sodium determinations were performed in the Evelyn photoelectric colorimeter on alkalinized, protein-free plasma supernates of heparinized blood.

Data are presented in the form of the actual excretion curves for all premature infants and the percentage dye retention at 45 minutes.

In normal adults, after a single injection of sulfobromophthalein sodium, the amount removed from blood is a function of plasma concentration, and when the logarithms of the sulfobromophthalein sodium values are plotted against time, they tend to assume a straight-line relationship. At low plasma concentration, however, the graph becomes curvilinear. When flattening of the curve occurs early and at high concentrations, liver function is abnormal.

Patients with hepatic disease may show the initial sharp slope characteristic of early rapid removal of dye followed by flattening of the curve at high plasma concentration indicating slower rates of sulfobromophthalein sodium removal.

Seven premature infants, 1,500 to 2,350 gm. and 18 to 28 hours of age, had excretion curves which were qualitatively similar to those of patients with hepatic disease but which differed in the absence of the initial phase of rapid sulfobromophthalein sodium removal. All had more than 15% retention at 45 minutes, and four had high plasma concentrations 4 to 18 hours after injection.

Of seven patients 1½ to 3½ days of age and weighing 1,500 to 2,170 gm., five had retention of over 4% at 45 minutes and flattening of the excretion curves at high plasma concentration. However, the initial sharp slope of rapid removal of dye now appeared in several.

By 1 to 2 weeks of age the curves approached the normal configuration. Of 10 premature infants 21 to 32 days of age and weighing 1,870 to 2,750 gm. all had less than 4% retention at 45 minutes, all showed the early phase of rapid fall in plasma levels, four had normal curves, and the other six still showed flattening but at somewhat lower plasma concentrations than previously.

Maturation of hepatic function appears to correlate with postnatal age and not with weight. Excretion curves assume the adult pattern at about 3 to 4 weeks of age.

The progressive maturation of hepatic function appears to be related to the increase in capillary vascularity of the liver that occurs with age, the rapid maturation of the Kupffer cells, which take up the dye and are responsible for the early phase of rapid removal of dye, and the somewhat slower maturation of the hepatic cells, which excrete sulfobromophthalein sodium into bile and which, if functioning abnormally, account for the flattening of the excretion curve.

DISCUSSION

DR. A. ASHLEY WEECH, Cincinnati: I was hoping that Dr. Obrinsky would try to relate his findings in the premature infant, No. 1, to those in the full-term infant. I judge from the circumstance that the increasing weight of the babies did not seem to be correlated very closely, certainly not so closely as age, with the liver dysfunction; that there would be not much difference if term infants were mentioned.

I should also like to hear him say a word about his thoughts concerning the relationship between this phenomenon and the physiological jaundice. I think one thing always stands out in my mind when I am wondering what is happening to circulation in the liver as a means of recovering function of the liver. The closing of the ducts is the thing that brings liver function back to normal. We must always remember in the study of physiological jaundice that there is a correlation between things that are found in the placenta and what happens to the baby later on and that there is a correlation between the level of bilirubin in cord blood and the course of bilirubinemia in the infant, all of which seems to be related to liver function, but which are related to something that happened before the time of birth.

DR. WILLIAM OBRINSKY (by invitation), New Orleans: We have not made studies on any full-term infants for several reasons, notably brevity of hospital stay. At Charity Hospital of Louisiana the mothers often go home at 18 hours after the birth, and the technical difficulties of six venipunctures immediately before discharge seemed great.

So far as the serum bilirubin is concerned, it has been shown by Dr. Mollison in his study of the sulfobromophthalein sodium test that there appears to be no correlation between the value of sulfobromophthalein sodium retained and the serum bilirubin. Indeed, in adults and in animals the injection of a high concentration of bilirubin does not alter the character of the curve one bit. The curve remains just the same.

I have a hard time in accepting the so-called changes in circulation as the cause of early abnormal curves. It seems to be possible that a gradual increase in the capillary concentration of the liver which occurs with increasing age may well account for this phenomenon.

Fourth Session

Thursday Afternoon, May 3

Etiology of Pulmonary Hyaline Membranes in Newborn Infants. DR. HERBERT C. MILLER, DR. FRANKLIN BEHRLE (by invitation), and DR. DAVID GIBSON (by invitation), Lawrence, Kan.

Hyaline membranes were produced in the lungs of young adult rabbits that were vagotomized in the midcervical region. The membranes appeared as early as four hours after vagotomy, and their incidence increased if the animal survived more than 10 hours after the operation. All animals died within 25 hours of the procedure.

The hyaline membranes were identical in appearance with those seen in the lungs of newborn infants. Also, the incidence of edema fluid, hemorrhage, and polymorphonuclear exudate in the air spaces of the lungs was the same in vagotomized rabbits and newborn infants when hyaline membranes were present.

The manner in which the hyaline membranes were produced in the vagotomized rabbits is not known, but presumably it is associated with the exudation of serum protein, blood, and polymorphonuclear cells.

Investigations have been made concerning the integrity of the vagus mechanism in the control of respirations in newborn infants. Tracings of the movements of the chest and abdomen suggest that there is at times a lack of synchronization of the movements of these two muscle groups—a finding which has also been described in vagotomized rabbits. Slow respiratory rates with an apneustic type of breathing have also been observed in newborn infants and vagotomized animals.

A study of the saliva flow and pharyngeal and laryngeal reflexes by direct laryngoscopy in newborn infants indicates that the cough reflex is often absent even in full-term infants and that gag and swallow reflexes are nonexistant in some premature infants along with a diminished saliva flow. The absence of these reflexes also suggests that certain central controls over respiration and the respiratory tree are impaired or lacking in some newborn infants, particularly premature infants.

It is suggested that hyaline membrane formation in newborn infants may be related to the impairment or absence of certain central nervous system mechanisms, possible vagal in location.

DISCUSSION

DR. STUART S. STEVENSON, Pittsburgh: I wonder if Dr. Miller has given much thought to the secondary drying effect of vagotomy on these rabbits. I wonder if he has tried introducing amniotic fluid into the rabbits and putting the rabbits into a high concentration of unhumidified oxygen.

DR. CLEMENT A. SMITH, Boston: I am glad that Dr. Miller a few years ago reopened this whole subject, because I think it has created much useful curiosity. One of the best steps forward is that which he is now taking in studying vagal and other nervous functions in the newborn infant, and especially in the premature infant, matters of which we know little.

His papers of a year ago started us restudying our material in Boston. My colleagues, Dr. Blystad and Dr. Landing, and I still hold to the thought that membrane formation is probably of amniotic fluid origin. This is, of course, extraordinarily difficult to prove, because it is a body protein, in any case, and where the source of that protein is, is very difficult to trace. I should also comment that my colleagues in the Harvard School of Public Health, Dr. Sarnoff and Dr. Whittenberger, who are doing a great deal of work with respiration now as a basis for use of their electrophrenic respirator, tell me that the rabbit is thrown into pulmonary edema somewhat more easily than other experimental animals, and that this is especially true of the vagotomized rabbit. So I would hope that this new approach could be tried on other animals.

Finally, I think perhaps the most interesting development of our renewed interest in membrane formation, which stems from Dr. Miller's work, is that the clinicians in the wards feel—and I think they are right—that they can pick out living babies who are going through the "hyaline membrane syndrome," or the resorption atelectasis, as Dr. Potter perhaps better calls it. We have learned that this is a self-limiting condition from which the baby, if it can be carried along four or five days, will, under those circumstances, survive and be perfectly normal; consequently, what was earlier considered more or less as an anatomical curiosity has grown to be thought of as a clinical entity, and a clinical entity which can be diagnosed, we believe, in the living patient.

DR. SYDNEY S. GELLIS, Boston: I think that Dr. Miller's theory is a very interesting one. I do not subscribe to his theory, chiefly on the basis of the work that we have done with diabetic mothers; we feel quite convinced that the prime cause of death in the live-born infant of the diabetic mother is hyaline membrane disease.

It would seem to us that if Dr. Miller's theory is correct, then the incidence of hyaline membrane disease might be expected to be equal in prematurely born infants of diabetic mothers whether delivered as normally or by Caesarean section. This is not true of our series. The high incidence in our series occurs in infants delivered by Caesarean section, and we believe that this syndrome, the hyaline membrane disease syndrome, is also responsible for the so-called Caesarean section syndrome.

The other thing some of us feel very strongly about is that the most important method of treating hyaline membrane disease is the use of fog or mist in an incubator. We feel that the period of respiratory embarrassment with this disease is markedly shortened and the severity of symptoms markedly decreased by the presence of mist in the incubator.

DR. CHARLES UPTON LOWE, Minneapolis: I should like to ask Dr. Miller whether he has stained other organs with the Schiff stain in order to find out whether they contain new carbohydrate-like material. The reason I ask is that we have stained rabbits' livers after cortisone therapy with this particular stain and have observed in these livers material which does take up Schiff's periodic acid stain. This material cannot be removed by saliva, although saliva would remove any glycogen present.

DR. STEWART H. CLIFFORD, Brookline, Mass.: I should like to congratulate Dr. Miller on his work and ask one question. I wonder if Dr. Miller has abandoned his earlier theory of etiology which, as I recall, was that the injury causing the membrane was some toxic substance that injured the epithelium of the alveoli. I believe, if I am correct, that Dr. Miller even felt that this unknown toxic substance might have been the cause of the premature labor.

DR. HERBERT C. MILLER, Lawrence, Kan.: We have had no extensive experience with the effects of drying or humidifying the air breathed by the laboratory animals. We have done a little, but it has been too little to give us any conclusions. The interesting thing about our animals at the present time is that if you put a vagotomized rabbit on a board and immobilize him for many hours, either with his head down or with his head up, the rabbit survives for several days instead of dying within the first 24 hours. The hyaline membranes will be there, but they will be there in lesser incidence; consequently, we have run across a problem which has delayed us in attempting to study the effects of drying or humidification, which we have done only to a slight degree. The same applies to studying the effects of oxygen.

I have the same feeling that Dr. Smith has, that some of these babies live, that if we can get them through the critical period they will eventually survive, and that they do not all necessarily have to die. Unfortunately, there is no sure way that I know of to diagnose this disease except at the autopsy table. We can only have a vague feeling that a baby is going through this procedure. Until we get a laboratory test that will be valuable during life, I think it remains a guess as to whether or not we are actually dealing with hyaline membrane disease in a baby who survives.

The Caesarean section question that Dr. Gellis raised is one that interests me. I am not sure we know all the answers to Caesarean section and its effect upon babies. I could think of many things that have been left uninvestigated. Perhaps it does have some very definite relation to this hyaline membrane, but it escapes me at the moment just what the relation can be.

We have not examined other organs with the Schiff reagent. We ran into a little difficulty with our Schiff reagent because, on subsequent examinations, the test did not work out as it had in the first instance. It is a rather difficult test to use; it is a little tricky, and we are in the process of attempting to straighten it out or a least straighten it out in our laboratory.

In answer to Dr. Clifford's question about the toxic substance and whether it is producing this hyaline membrane, I have not abandoned the possibility that there may be some toxic substance working on the lung. Where the toxic substance is coming from, I don't know. I do not see how we can abandon that concept as long as we know that hyaline membranes apparently of the same nature are found in patients with pneumonia and with many other conditions in which the opportunity for toxic agents to act is considerable.

I have abandoned for the present the theory that whatever it is that produces hyaline membrane also starts the premature labor.

As to the question of whether or not this is aspirated amniotic fluid or something else, I simply feel that no number of Brighton punches is going to settle that question.

Observations on the Use of Soy Bean Trypsin Inhibitor in Stool Trypsin Determination. DR. DOUGLAS E. JOHNSTONE (by invitation), Baltimore.

The purpose of this study was to elucidate some of the factors responsible for the gelatin-liquefying capacity of feces of normal children and to throw some light upon factors which might cause or prevent falsely positive reactions on the x-ray film test for fecal trypsin in children suffering from cystic fibrosis of the pancreas.

Of 137 patients with cystic fibrosis of the pancreas given 209 x-ray film tests for fecal trypsin, 59.9% had falsely positive reactions, even when the patients were not receiving pancreatin therapy. However, none of the specimens gave a positive reaction in a dilution of greater than 1:100. Stool cultures of these patients revealed that bacterial gelatinase (produced by Pseudomonas aeruginosa, Proteus ammoniae, Proteus morganii, Proteus vulgaris, Aerobacter cloacae, and chromogenic bacilli) was present in 98% of 48 stools giving falsely positive reactions, but in only 7% of those giving negative reactions. Gelatin liquefaction by concentrated solutions of bacterial gelatinase could be inhibited by antigelatinases. Attempts with use of these same antigelatinases to inhibit gelatin liquefaction by feces of patients with cystic fibrosis of the

pancreas who were harboring bacterial gelatinase produced equivocal results. Soy bean trypsin inhibitor consistantly failed to prevent gelatin liquefaction by these same specimens. Gelatin liquefaction by crystalline trypsin and suspensions of normal feces can be inhibited completely by soy bean trypsin inhibitor but not by antigelatinases thus far tested.

To determine whether false positive fecal x-ray film reactions might be obviated by a simple dilution of the fecal suspension, approximately 8,000 x-ray film tests were done by a modified Schwachman technique on 826 fecal specimens of 184 normal children, infants, and newborn infants, both full term and premature. Fifty-four per cent of meconium specimens produced gelatin liquefaction in a dilution of 1 : 100 or greater; 95% of subsequent stools in the premature infants, full-term newborn infants, and other groups were similarly positive in a dilution of 1 : 100 or higher. Admittedly, however, only small numbers of older children, whose stools seem to have less gelatin-liquefying power, were studied. Fecal cultures of these normal specimens revealed that approximately 21% harbored gelatin-liquefying bacteria. Ps. aeruginosa and Proteus were the most frequently encountered organisms.

An effort was made to determine if there existed a stoicheiometric relationship between the amount of tryptic activity present in a solution and the amount of soy bean trypsin inhibitor required to inhibit this tryptic activity. Eight attempts to titrate varying amounts of crystalline trypsin against varying amounts of soy bean trypsin inhibitor were made. From the several curves thus obtained, it was found that 1 mg. of soy bean trypsin inhibitor inhibited approximately 2 mg. of crystalline trypsin.

An attempt to apply similar titration techniques to stool were less successful or consistent. When varying amounts of soy bean trypsin inhibitor were added to different dilutions of stool suspensions, there was not constant a relationship between the amount of inhibitor required to prevent gelatin liquefaction and the amount of feces present in the preparation. Consequently, although soy bean trypsin inhibitor may be used to differentiate qualitatively fecal pancreatogenic trypsin from bacterial gelatinase, a suitable method of quantitative estimation of trypsin by the inhibitor technique is not yet available.

DISCUSSION

Dr. Paul Patterson (by invitation), Boston: In the development of this technique by Schwachman and myself, our desire was one of simplicity of the screening test of pancreatic fibrosis. Contrary to the findings that Dr. Johnstone has presented, we have not had quite that many false negatives.

I should like to know whether he did follow our technique in doing the tests and left the drop of feces uncovered. When we were attempting to simplify this, we started with a very complicated method which got more complicated as we went along. If you do cover it with nothing but a drop of water on gelatin film, you can get a positive reaction.

The role of pH in enzyme activity is important. Realizing that pepsin and trypsin are prolific enzymes, it must be a matter of pH range; whether they act or not is a matter of pH coming into play.

Another fact of importance in stool trypsin testing in pancreatic fibrosis is the realization that you may have trypsin present in the duodenal fluid of patients with pancreatic fibrosis. If you make the diagnosis of pancreatic fibrosis by the absence of trypsin alone, you are going to miss from 15 to 25% of cases. We demonstrated last year by the use of the viscosity measurement that you can have practically normal trypsin and still have pancreatic fibrosis, especially in infants, and as the infants mature, the trypsin will disappear.

If this bacteria should be producing enzymatic activity in the fluid, we should find bacteria in a concentration to do that. In checking the stools, as the children become older, we find the reaction for stool trypsin becomes more and more negative. As the child reaches 10 years and above, we have more and more negative stool trypsin reactions. At that stage, you find actually the quantitative bacteria in the stool should increase. As that progresses, the stool trypsin reaction tends to become negative. In fact, you have less false positives; consequently, in evaluating these, it might be stated that we have at Children's Hospital mention of 98 cases of pancreatic fibrosis. These positive reactions were only in the infant group, and we had 16 positives.

Because in the infant group there may still be trypsin present, when we did stool trypsin determinations and two of those 22 determinations gave positive results, we included the two

patients in the series. For these reasons, I should very much like to have Dr. Johnstone explain this technique in detail and mention how he did these tests, whether he followed our original directions, kept the feces off of the gelatin film, and if he did not realize that we may have patients who have trypsin coming down from the bowel perfectly normally as the case of pancreatic fibrosis progresses.

DR. STUART S. STEVENSON, Pittsburgh: I should like to know whether Eastman film or du Pont film was used. We found a higher percentage (I can't give you the figure offhand) of false positive reactions when following Dr. Schwachman's technique and using du Pont film.

DR. DOROTHY H. ANDERSEN, New York: It seems to me that the number of false positive reactions has altered somewhat since the first year in which we used this test. When the test first appeared, it seemed to be a perfect solution to the very difficult problem of diagnosing these cases. During the first year or so in which we used it, we found very few false positives and good correlation with other methods of diagnosis.

The period during which the incidence of false positives was observed to increase coincided with the time that penicillin first became readily available. Since 1944, when we first had free access to penicillin, there has been a very large percentage of the children with fibrocystic disease in whom the flora of the respiratory tract has changed. Practically all of them have acquired Pseudomonas in the respiratory tract and not uncommonly in the feces. Pseudomonas seems to be one of the organisms that most consistently give a positive film reaction. This has complicated the interpretation of the film test, and it has made us feel that the film test is of very little practical value unless modified as Dr. Johnstone has suggested. This has been our experience for the last five years.

His observations on the presence of Pseudomonas in the duodenal juice reopens the question of whether the finding of positive reactions for trypsin in the duodenal juice in cases that are clinically doubtful really means that pancreatic trypsin is present or whether a bacterial gelatinase may not be the proteolytic agent. There have been several children that have died with the clinical and postmortem findings of fibrocystic disease who certainly before death gave high assay figures for trypsin in the duodenal juice.

This is certainly a field which should be explored further. The rapid increase in the use of antibiotics and the consequent alterations of the respiratory flora followed so soon after the introduction of the film text that interpretation of the data was made rather difficult.

DR. DOUGLAS E. JOHNSTONE (by invitation), Baltimore: I want to thank you for your kind comments and very provocative questions. I certainly want to emphasize that in no way do I detract from the fine work Dr. Schwachman and Dr. Patterson have done. I think theirs is a very fine idea, and I think, with a few modifications, it is a very useful technique.

In terms of what technique we used, we tried to follow Dr. Schwachman's technique to the letter, with perhaps one or two exceptions. First, I believe in Dr. Schwachman's original description he suggested that at the end of one hour of incubation one ought to wash off the film with water and with gentle rubbing. Gentle rubbing alone can give a false positive result, and we did not do that. We merely washed off with water.

We did cover the x-ray film with a Petri dish and ran controls and found that the water alone did not liquefy the x-ray film. It is interesting, in connection with water, that one of the New Orleans group said that same thing to me, that water would do it. He cultured the water, and he found a gelatin-liquefying bacteria in the tap water in his particular hospital in New Orleans; consequently, the theoretical possibility of contamination is still there. I don't imply that the tap water in Boston has Ps. aeruginosa in it, but while we were working in Dr. Anderson's laboratory, some of our diluent did get contaminated by Ps. aeruginosa, so we know it can happen.

With regard to covering or not covering the x-ray film, I think it is very important and necessary to cover it. We take the piece of x-ray film and make a circle with wax crayon on it and put our test solution on the circle and then cover with the Petri dish. We found that some of the house staff doing this test would report negative reaction, and we could take the same piece of dried x-ray film and put a drop of distilled, bacteria-free water on it and get a positive reaction after incubation. They would take the same film from the same source and use distilled water

as a control and not get a positive reaction. I think actually it may dry out if we do not cover it, and a false negative reaction may thus be obtained.

I am perfectly in accord with the other factors Dr. Patterson mentioned, such as pH. When we tried to find out, in our first studies with Dr. Neter, if we could prevent this action of bacterial gelatinase by simply adding aureomycin to the substrate, we found that aureomycin alone would not do it. If we added not aureomycin by itself but aureomycin hydrochloride, so that the pH of the solution went down below 5.2, then we could stop the gelatin-liquefying activity of this gelatinase.

We are now, in an attempt to maintain a rather constant and uniform and normal pH of our substrate, using a barbiturate buffer and maintaining a pH of approximately 8.0, which we have checked, and that, I feel, should be the substrate that the feces are mixed with. However, sterile, distilled water, if it is not too acid, usually works. Most of our normals were worked out on that basis.

I agree there may be such a thing as partial cystic or precystic conditions in which one finds some trypsin. However, the duodenal juices of these patients haven't been examined for gelatin-liquefying bacteria.

I think Dr. Anderson's point is very good, that some of these patients' duodenal juices may not actually have trypsin, although one, I think, can verify it very easily by using soy bean trypsin inhibitor.

Although many people think gelatinase produced by bacteria is very similar to trypsin and has a substrate grouping very similar, it can be differentiated from trypsin by trypsin inhibitor.

Bacteria not only can but do cause falsely positive reactions; these strains of bacteria—and Dr. Nedder and I at Buffalo studied over 150 of them—vary tremendously in their gelatin-liquefying power: one strain in its 24-hour broth culture, which is diluted to 1: 100,000, will give a positive x-ray film reaction; others undiluted will just barely give a positive reaction.

I agree that constipation certainly can cause a falsely negative reaction. We know that patients who have megacolon before they are operated on will have a falsely negative x-ray film reaction very frequently, provided their feces don't contain gelatinase, but after you have operated upon these patients and eliminated the factor of stasis of feces in the colon, these patients have a fairly normal reaction; this we have seen on several occasions.

With regard to Dr. Stevenson's suggestion for use of the Eastman film, I am more inclined to agree with Dr. Patterson and Dr. Schwachman on this point. We have shown, using Eastman film, du Pont film, and Hammer panchromatic portrait film, that it makes a big difference what kind of film you use. With the same stool specimen or the same dilution of trypsin, one can get a positive reaction at a much higher dilution with one type of film than with another. We have constantly used the Eastman Blue Brand x-ray film for consistency. It may be that you don't get the full trypsin activity on the du Pont or the other film.

All these cases mentioned were diagnosed, most of them by Dr. Anderson, some in Buffalo, and had routine diagnostic work-ups done. Many of them, of course, had amino acid tolerance tests and other tests to substantiate the diagnosis.

The point about penicillin that Dr. Anderson brings up is a very fascinating one, and we could spend the afternoon on it. Briefly, there appears to be a conversion of the normal bacterial flora, and we showed in the original study of these 78 patients that there was a very nice correlation; if we studied the flora before the patient received penicillin and afterwards, there was a very strong correlation between the conversion of the normal flora from Gram-positive organisms to Gram-negative organisms, frequentiy Ps. aeruginosa, and with this correlation one could see a great increase for the particular patient of falsely positive fecal x-ray film reactions.

I think that just simply diluting the stool from 1: 100 will rule out most of these false positive reactions.

Absorption of Alpha-Tocopherol and Tocopheryl Esters by Premature and Full-Term Infants and Infants and Children in Health and Disease. LLOYD J. FILER JR., PH.D. (by invitation), DR. STANLEY W. WRIGHT (by invitation), DR. MARY-PARKE MANNING (by invitation), and KARL E. MASON, PH.D. (by invitation), Rochester, N. Y.

Serum tocopherol (vitamin E) levels following oral doses of alpha-tocopherol or tocopheryl esters at 20 mg. per kilogram of body weight were determined every three hours for a 12-hour

period by the microchemical method of Quaife and co-workers (*J. Biol. Chem.* **180**:1229, 1949). The resulting data when plotted yielded a "tolerance curve" with a maximum at nine hours and a measurable area under the curve.

Premature infants (42 observations) were found to absorb vitamin E as well as full-term infants (15 observations) when compared on the basis of area under the curve for a 12-hour period. This is in marked contrast to the diminished ability of the premature infant to utilize vitamin A and fats.

In a series of 29 infants, only those disease states diagnosed as fibrocystic disease of the pancreas, diarrhea, and cirrhosis were characterized by flat tolerance curves.

In a series of 14 children, patients with celiac syndrome and lupus erythematosis were noted to absorb tocopherols poorly. Metabolic disorders with associated hypercholesteremia were observed to give abnormally high values for the area under the curve.

A comparison of vitamin A absorption with tocopherol absorption in a series of 10 observations indicated that patients responding poorly to one test did poorly in both.

DISCUSSION

DR. HARRY WAISMAN, Chicago: I think this excellent work that has been done has a bearing on one other factor, and this is that some workers during the past year have suggested that vitamin E be given for retrolental fibroplasia. I think if the premature infant is able to do as well as this in absorbing vitamin E, it might be worth while hearing from the speaker whether this incidental observation was done on premature infants.

DR. PAUL PATTERSON (by invitation), Boston: I should like to ask the author whether, by chance, he ran the vitamin A tolerance test at the same time with the vitamin E test and whether or not he used a natural tocopherol, laboratory experiments showing that in rats you can definitely increase the vitamin A level in the blood. You can use possibly an antioxygen action on vitamin E and thus increase the blood level of vitamin A.

In studying a group of adults who had aspermia, in Boston, we gave these men high doses of vitamin A and also gave them high doses of natural tocopherol, and we noted a definite increase in the level of vitamin A in their blood. It would be interesting to know whether he used natural tocopherol and whether he got an increase in the blood level of vitamin A at the same time.

DR. BAIN, Brooklyn: We administered both vitamin A and vitamin E in single preparations and observed the same improvement in the curve of vitamin E that we did with vitamin A. Vitamin A was given routinely, at the suggestion of Dr. Owens, as a possible prophylaxis when we suspected retrolental fibroplasia might develop, but during this treatment fibroplasia developed, in several of the infants, and we discontinued it.

DR. LLOYD J. FILER JR., PH.D. (by invitation), Rochester, N. Y.: In our laboratories we have not concerned ourselves with the problem of retrolental fibroplasia, inasmuch, as Dr. Waisman said, this is a type of work that had to be done and we went ahead and did it.

With respect to the interaction of vitamins E and A, there is no doubt that the antioxygen effect of vitamin E does enhance or increase the blood level of vitamin A. The tocopherols that we tested were natural tocopherols, furnished to us by Distillation Products, of Indiana.

We did calculate some coefficients of correlation between vitamin E and carotene and were able to show a positive coefficient of correlation of $+0.55$, meaning if one enriches the blood in tocopherol, one enriches the blood in carotene. We did not carry out our tests of vitamin A and vitamin E absorption simultaneously. They were done within a matter of a few days of each other.

A Study of Light-Induced Epilepsy in Children. DR. H. M. KEITH (by invitation), DR. R. A. ALDRICH (by invitation), DR. D. DALY (by invitation), DR. R. G. BICKFORD (by invitation), and DR. R. L. J. KENNEDY, Rochester, Minn.

Twelve children who suffered from convulsive disorders were found to show electroencephalographic changes after flickering light stimulation. In the majority of these clinical seizures coincided with electroencephalographic findings.

In the case of one patient, clinical attacks as well as electroencephalographic changes occurred with visual stimulation by fine mesh patterns. This sensitivity for patterns was specific in the

sense that floral or large designs did not induce symptoms or electroencephalographic abnormalities.

The data from these studies are discussed from the clinical and electroencephalographic standpoint. Emphasis is placed on these phenomena as sensory trigger mechanisms in the production of convulsive attacks and on the need for their recognition in planning effective treatment.

DISCUSSION

DR. SAM KARELITZ, New York: I have never observed the phenomenon that Dr. Aldrich described, but I should like to call attention to a child with an ataxia ascribed to a condition referred to as electric chorea of Dubini. This 19-month-old child awoke one morning with a diffuse ataxia, which continued unabated for a long time. It was noticed that when a light was flashed into the child's eyes, she would go into a generalized spasm, and the nystagmus which started with the onset of ataxia became very much worse for the moment. We could demonstrate this reaction regularly and reproduce it by a sudden jarring noise. There are very few such cases reported. We have a follow-up of about two years on this child. There has been spontaneous improvement, with the result that the child can now do many of her daily chores for herself, but the ataxia, nystagmus, and light sensitivity continue. As I recall, the electroencephalographic pattern was that of a diffuse encephalopathy rather than that of epilepsy, but unfortunately we did not know about the observations reported by Dr. Aldrich and never did have electroencephalographic tracings made at the time of ocular stimulation.

DR. SAMUEL LIVINGSTON, Baltimore: I should like to relate some experiences we have had with several patients who suffered with so-called photogenic epilepsy.

The first patient was a 32-year-old white man who had his first convulsive seizure at 18 years of age. At that time, he was driving his automobile through the country on a very bright sunny day. He said that as he was riding along, the sun flickered through the tree branches and "made him feel funny in the eyes." The next thing he remembered was that he was in a hospital. He was told that he had had a convulsion and "ran his car up a tree."

We saw him for the first time about two years ago. His complaint at that time was that the sunlight bothered his eyes and caused him to have convulsions. He was admitted to the hospital and studied completely. All routine examinations, including a routine electroencephalogram, showed normal results. When the patient was stimulated with a flickering light, he had a clinical seizure. An electroencephalogram performed at this time showed spike and wave activity which appeared simultaneously with the clinical seizure.

The patient was then stimulated with flickering colored lights: red, blue, and green. It was observed that he was extremely sensitive to the red flickering light. The slightest degree of stimulation with the red light caused the patient to have both a clinical seizure and also specific evidence of epilepsy in the electroencephalogram.

A pair of glasses with a lens which filtered out red light was prescribed for this patient. Since he has been wearing these glasses he has not had a convulsion.

We have also seen three children during the past year who had their first convulsive seizure while watching a television show. Each patient spontaneously told us that the "television screen" was flickering at the time the children were watching the show. Although we were unable to produce a seizure, either clinical or in the electroencephalogram, with the flickering light, it is felt that the flickering sensation produced by the television may possibly have acted as a trigger mechanism in the precipitation of the initial convulsion. In all three of these patients recurrent convulsions (epilepsy) have now developed.

We also had another patient, an 8-year-old girl, who has been having recurrent seizures for some time. The mother gave the following history: "My daughter only has spells in the morning when she goes off to school. I think she is faking because she does not want to go to school." A thorough history revealed that this child had her convulsions as soon as she walked out of her house on bright sunny days. She did not have seizures on cloudy days.

We were unable to produce a seizure, either clinical or electroencephalographic, with the flickering light. We did, however, prescribe dark glasses for this child, which has resulted in a marked improvement.

DR. MYRON E. WEGMAN, New Orleans: I should like to ask the authors whether they made any study of the eye movements in these patients during the exposure to the light stimulus. In some of the techniques described, as well as in the television-induced seizure described by Dr. Livingston, alternating movements may be shown as well as alternation in the light. This involves the concept of "optic nystagmus." Some years ago I had occasion, with Dr. J. C. Fox, to study the eye movements in postencephalitic Parkinsonism and found that as rapidly alternating stimuli were given to the eyes cerebral deterioration was accompanied with much more difficulty in handling the rapid alternation of stimuli. I wonder if that could be a factor here.

DR. R. A. ALDRICH (by invitation), Rochester, Minn.: I should like to thank the discussants for their comments.

Dr. Wegman, these children have been well studied from the neurologic standpoint. The boy with the pattern sensitivity had an IQ of 122 and showed no evidence of any sort of encephalitic component or cerebral damage.

I do not think we could say from our observations that there is any evidence of difficulty with the eye movements.

There is one thing I wanted to add. We do not have any good statistical evidence on how common light sensitivity is. The procedure is easy to use as a routine, taking only a few minutes of extra time in the laboratory, and for this reason statistical data should be available soon.

Chemical Growth in Man. GILBERT B. FORBES, Dallas.

Mathematical descriptions of the growth of organs in a number of species have been greatly simplified through the use of the equation $y = bx^k$, where y stands for the weight of an organ and x for the total body mass. The exponent k, which is a ratio of differential growth, is the slope of a log-log plot of the two variables and is constant whenever the relationship is a linear one.

It was first shown by Needham that the chemical constitutents of the animal body could be described in this manner, and Iob and Swanson have calculated differential growth ratios for a number of chemical elements in the human fetus. The availability of radioisotopes has made it possible to ascertain for the first time certain aspects of the chemical composition of the living human subject. Using data obtained by the isotopic dilution method, equations of the general form given above have been derived for the relationship of total body sodium (Arthor's data), and total body potassium and total body water (data of F. Moore and associates) to total body mass in the postnatal human. It has been found that these equations are applicable over a large range of body weight and therefore allow one to predict body composition for normal subjects of any given body weight and to anticipate mineral retentions due to normal growth. Interesting comparisons can be made between the various chemical elements for which such equations are available.

DISCUSSION

DR. WILLIAM W. SWANSON, Chicago: I should just like to commend the author on the excellent presentation. It seems to me that whatever data Dr. Forbes has obtained from my figures on chemical composition have been presented better than in my earlier papers.

Report on a Disorder of the Skeleton Resembling Rickets, Associated with Loss of Teeth and Deficient Alkaline Phosphatase Activity in a 2-Year-Old Child. DR. EDNA H. SOBEL (by invitation), Cincinnati; L. C. CARK JR., PH.D. (by invitation), and DR. M. ROBINOW (by invitation), Yellow Springs, Ohio.

The patient is a 2-year-old girl whose skeleton has become progressively deformed and who has lost most of her deciduous teeth. Her general health is good; stature is within normal limits, and the history reveals no outstanding dietary deficiencies. Roentgenograms showed poor mineralization of the skeleton and teeth, with symmetrical focal defects in the metaphyses of the major long bones. The skull and vertebrae were not abnormal. The serum calcium was normal (9.8 to 10.3 mg. per 100 cc.). The serum inorganic phosphate (5.3 to 6.0 mg. per 100 cc.) and red cell organic acid-soluble phosphate (total 61 mg. per 100 cc., adenosine triphosphate 13

mg. per 100 cc.) were at upper normal levels. The alkaline phosphatase activity of the serum was very low (0.8 to 1.3 sodium paranitrophenylphosphate [Bessey-Lowry] units). The patient's serum did not inactivate alkaline phosphatase of normal serum. Chemical analyses revealed no evidence of poisoning by heavy metals, beryllium, or fluoride. The father's serum alkaline phosphatase is also low (1.01 sodium paranitrophenylphosphate units), while that of the mother is normal (2.38 sodium paranitrophenylphosphate units).

Biopsy specimens of liver and ribs were obtained. The alkaline phosphatase activity at the costochondral junction was 75.6 sodium paranitrophenylphosphate units, as compared with 510 and 645 for two children without skeletal disease and 1,190 for a patient with active rickets. The liver alkaline phosphatase activity was 49.2 sodium paranitrophenylphosphate units (for two controls it was 109 and 500 respectively; in one case of active rickets it was 233). Rathbun (*Am. J. Dis. Child.* **78**:822 [June] 1948) has reported a similar relationship between low serum and tissue alkaline phosphatase activity in a patient with skeletal disease. Schneider and Corcoran (*J. Lab. & Clin. Med.* **36**:985, 1950) reported two brothers with skeletal deformities and low serum alkaline phosphatase. Microscopic examination of the costochondral junction showed the architecture of rickets (Dr. Edwards A. Park, personal communication).

Neither purified growth hormone (Armour) nor thyroid hormone influenced the plasma alkaline phosphatase when they were given in an attempt to stimulate osteoblastic activity. A preliminary trial with large doses of vitamin D suggested that this too would be without effect. Rachitic rat bone, when incubated with the patient's serum, showed less calcification in the cartilage than was shown by the same cartilage incubated in the serum of normal children (these studies were performed by Miss Phyllis Fox, Fels Research Institute for the Study of Human Development). In view of the normal calcium and phosphate content of the patient's serum, the lack of calcification of rachitic cartilage was unexpected and will be studied further.

The occurrence of rickets with normal serum calcium and phosphate concentrations and very low alkaline phosphatase activity in the bone and serum favors the hypotheses that the skeletal disorder is due to a local disturbance and that this may be related to a deficiency of alkaline phosphatase activity in the growing bone. While the precise role of alkaline phosphatase in the formation of bone is not clear, the findings in this patient suggest that growing bone may require the presence of alkaline phosphatase for normal calcification.

DISCUSSION

Dr. Edwards A. Park, Baltimore: I shall confine my discussion to the description of the bone which Dr. Sobel sent me. The lesion in the bone was that of ordinary deficiency rickets, and at no point did it differ from that condition. The osteoblasts in the bone seemed to be normal in number, and the morphologic picture seemed to be normal. Many of them were obviously producing bone matrix, and there was no evidence whatsoever of any deficiency in their power to produce bone matrix. This was proved by the broad osteoid borders of the trabeculae, which must have been produced by the osteoblasts recently.

The bone was not stained for phosphatase, and it is quite possible that the power to produce matrix substance on the part of the osteoblasts was preserved, whereas the power to produce phosphatase was lost, or at least was lost in part.

I think that Dr. Sobel's case is exceedingly interesting, and again, as she remarked, it seemed as if this must be a form of rickets which certainly has never been adequately described, in which the disturbance in calcification must depend upon the absence of some local factor in the cartilage and in the bone, and the fact that the phosphatase concentration is so low would lead one to suspect that the factor which was lacking was connected in some way with or was the alkaline phosphatase itself.

Dr. Samuel W. Clausen, Rochester, N. Y.: We have observed three cases of this syndrome in one family, that is, all the children were affected in just the same way as Dr. Sobel's patient, so that possibly there is a genetic factor involved here rather than a factor of toxicity.

I might say that in our case we gave vitamin D in such quantities as to produce toxic hypercalcemia, and nevertheless no healing occurred.

Dr. B. Kramer, Brooklyn: Dr. Sobel and her co-workers have described a new form of endogenous rickets due to a defect in a factor in bone which seems to be enzymic in nature. That

local factors play a part in determining mineralization of cartilage and osteoid is indicated (1) by the highly selective character of the bone salt deposits, (2) by studies on transplanted cartilage in which only that cartilage containing phosphatase undergoes mineralization, and (3) by studies on in vitro calcification in which the process of mineralization can be inhibited or even abolished by the addition of chemicals which injure vital processes. The local factor of calcifying tissues seems to be enzymic in character. So far, two such enzymes have been correlated with calcification: (1) the alkaline phosphatase of Robison and Rosenheim and (2) the phosphorylaze of Gutman and Yu. Dr. Sobel has demonstrated a marked deficiency of phosphatase activity not only in the cartilage and in bone but also in other tissues. In other words, we are dealing here with a systemic defect. Dr. Sobel was unable to demonstrate poisoning by the usual substances that are known to affect calcification, such as heavy metals, beryllium, or fluoride. If such substances did exist in the serum, they were apparently not present in sufficient excess to affect the phosphatase activity of normal serum.

It is interesting to note that rachitic cartilage failed to calcify when incubated in the patient's serum, although the calcium times phosphorus product in the serum was normal, and no doubt plenty of phosphatase must have been present in the rachitic cartilage.

Dr. Sobel is to be congratulated on the reporting of an interesting case beautifully worked up.

DR. EDNA H. SOBEL (by invitation), Cincinnati: I should like to thank Dr. Park again for his extreme kindness and helpfulness in our effort to elucidate the problem presented by this child.

I was very much interested to hear Dr. Clausen report three cases in one family. We have certainly thought that it was possible that there might be a genetic factor in the disorder. The mother of our second patient also has low serum alkaline phosphatase activity. We are, however, a little intrigued by the suggestion of possible exposure to beryllium, although we do not intend to propose that this may be responsible for the disorder; we will investigate it further.

Dr. Kramer again points out that the role of alkaline phosphatase in in vitro calcification has never been clarified. Miss Phyllis Fox, of the Fels Research Institute for the Study of Human Development, has done some in vitro studies in relation to that problem. Rachitic rat cartilage was incubated with the patient's serum. No calcification occurred in the cartilage, although the same cartilage calcified in normal rat serum.

While it is true that there is some calcification in the child's skeleton despite the reduced amount of alkaline phosphatase activity, the degree of mineralization is far from normal. We might mention that the minimal alkaline phosphatase activity which was present in the serum apparently had its origin in the bone, since it showed 50% inhibition with taurocholate.

Factors in Hypocalcemia of the Newborn: A Longitudinal Study of the Chemical Composition of the Serum in Full-Term and in Premature Infants in the Neonatal Period. DR. ERIKA BRUCE and DR. DAVID H. WEINTRAUB (by invitation), Buffalo.

The finding of frequent cases of hypocalcemia among newborn infants who were either premature or seriously ill stimulated the following questions:

1. What are the normal fluctuations of the serum calcium level in full-term and premature infants in the course of the neonatal period?

2. Which factors influence the serum calcium level?

3. Can the infants' symptoms be correlated with the calcium level, considering also such other influences as the serum potassium level and pH?

In order to answer some of these questions, 50 premature and 21 full-term newborn infants were studied. Eleven of the premature infants received human milk, the others various cow's milk formulas. Vitamin D administration was started for all premature infants on the eighth day of life. Calcium, phosphorus, phosphatase, pH, carbon dioxide content, and potassium were determined, in addition to in cord blood, in venous blood before the first feeding and at intervals thereafter within the first to third weeks of life.

In the full-term infants the mean calcium level was 9.2 mg. per 100 cc., with little fluctuation. Only four full-term infants had levels below 8.5 mg.; two of these were infants of diabetic mothers, a third one had marked hypoglycemia and convulsions.

The mean calcium level of the premature infants was 8.2 mg. per 100 cc.; the fluctuations were much wider, 44 of 50 infants reaching levels below 9 mg., 18 below 7 mg. The calcium level usually rose to above 9 mg. spontaneously within 10 days.

There is a striking contrast between full-term (mode 9 to 10) and premature (mode 7 to 8) infants in the distribution of minimum calcium values attained by each infant.

With respect to the diet, in 42 of 71 babies the lowest level was observed before feedings had been started. Only one infant reached the minimum level while on human milk; of the cow's-milk-fed infants, about 40% reached the minimum level while on this feeding. The difference between infants fed human milk and those fed cow's milk is of doubtful statistical significance.

Phosphate levels were investigated (1) in relation to the diet, (2) in relation to the calcium level. There was no difference between full-term and premature infants either in the mean inorganic phosphorus level, 7.5 and 7.6 respectively, or in the incidence of maximum levels attained (mode 7.5 to 9). There was a statistically highly significant influence of the diet: most of the infants fed human milk had the highest phosphorus level before feeding; most of those fed cow's milk, after feeding had been started.

The correlation of calcium and phosphorus levels in individual samples shows an extremely wide scatter. The correlation factor is -0.31.

In individual infants the curves of calcium and phosphorus levels run as often parallel as in opposite directions.

The mean alkaline phosphatase level was 6.34 Bodansky units. Only one infant had a phosphatase activity above 12 Bodansky units persistently for 12 days. This infant had profound hypocalcemia during the same 12-day period. His bones and those of another infant had striking translucent zones near the ends of the metaphyses roentgenographically.

Six infants were ill with other disease; all of them had calcium levels below 8 mg. per 100 cc. Considering some data in the literature (von Sydow), it is suggested that rickets may play a role in the hypocalcemia of some infants, particularly sick ones.

The levels of calcium and phosphorus in the cord blood bore no relation to subsequent values.

Study of the pH and carbon dioxide content revealed 26 cases of respiratory and some of metabolic acidosis which had no obvious effect on the calcium level.

The potassium levels were almost all between 4 and 6 mEq. per liter. No relation to the calcium levels was evident.

No relation could be found betweeen the serum calcium level and either the birth weight or the rate of weight gain.

The commonly recognized symptoms of tetany were rare among the infants with hypocalcemia. Two hypocalcemic infants died with signs suggestive of tetany.

DISCUSSION

DR. W. MCCRORY, Philadelphia: I should like to express my interest in the studies Dr. Bruck has demonstrated here; also, I should like to admit that I am rather overwhelmed by the amount of material covered. In the introductory statement, 29 patients with hypocalcemia were listed, and in only six were there no associated complications. This would leave us with 23 potential causes of hypocalcemia in newborn infants.

Most of us, I believe, in considering neonatal tetany, at least the disease I presented data on last year, limit ourselves to the less confusing part, and that is the disorder in the infant without other complications who does demonstrate hypocalcemia and convulsions. Time does not permit a discussion of the multiple factors mentioned here. I feel that the data presented again point out that though no direct relationship can be observed between serum calcium and phosphorus levels, there does seem to be a relationship between intake of phosphate and level of serum in organic phosphorus. There seems to be a time relationship as well, as was seen in one of the figures. The calcium and phosphorus values might be studied more properly in terms of the day of life of the infant and his calcium and phosphorus intake rather than by analyzing a mass of such data in an attempt to observe a simple relationship between calcium and phosphorus levels in serum. Obviously, there is much more to be done by many people, and I feel this was a very worth-while presentation.

Quantitative Approach to Separation of Lipid Mixtures. Dr. Edward H. Ahrens Jr. and Lyman C. Craig, Ph.D. (by invitation), New York.

Clinical investigations of lipid metabolism are hampered by lack of fundamental studies of chemical structure and physical properties of pure lipid compounds. Indeed, the indefiniteness of basic data gives rise to many of the uncertainties of the methodology of the clinical laboratory. The primary difficulties in this field have been produced by the strong association tendencies which hinder complete extraction of lipids and their subsequent separation into individual pure components. The present report demonstrates that these forces can be overcome by countercurrent distribution of lipid mixtures between immiscible solvents.

The countercurrent approach has made possible the quantitative separation of 5 gm. of mixed lipids from 1 liter of human plasma into 3 main groups: phospholipids, cholesterol, and triglycerides plus cholesterol esters. Fractionation of the third group is now in progress. The opportunity to characterize the composition of these groups and their components separately is now at hand for the first time. Experimental results of these fractionations are presented.

Experience with a wide variety of lipids permits the conclusion that countercurrent distribution, which is simultaneously analytical and preparative, presents the possibility of all-inclusive analysis of extremely complex mixtures of lipids. Attainment of single pure compounds from these mixtures is essential to progress in the lipid field.

Circulatory Dynamics in Complete Transposition of the Great Vessels: Physiologic Considerations with Report of Four Cases. Dr. Richard E. L. Fowler (by invitation) and Dr. Nelson K. Ordway, New Orleans.

Circulatory hemodynamics in complete transposition of the great vessels has been investigated by means of cardiac catheterization in four infants ranging in age from 3 to 7 weeks. Three of these cases were thought to represent the anomaly in its "pure" form, i. e., associated with patent foramen ovale and patent ductus arteriosus only; one appeared to be combined with a ventricular septal defect.

Pressure tracings in the "pure" type revealed in all cases a higher pressure in the left atrium than in the right, suggesting that a shunt at the atrial level would be from left to right. In the single case associated with a ventricular septal defect, there was no clear-cut difference in atrial pressures. Right (systemic) ventricular pressure exceeded left ventricular in the two cases of the "pure" type in which this comparison could be made, as well as in the case associated with ventricular septal defect. Aortic pressure therefore should exceed pulmonic, resulting in a flow of blood from aorta to pulmonary artery through the patent ductus, if present.

Blood oxygen determinations revealed a single left-to-right shunt at the atrial level in two of the "pure" cases and simultaneous left-to-right and right-to-left shunts in the other case. In two cases samples of blood were obtained both from the right side of the heart and from the femoral artery; these showed the same oxygen content, indicating that no oxygenated blood was entering the aorta between these two points, i. e., through a patent ductus from the pulmonary artery. In the case associated with a ventricular septal defect there were simultaneous left-to-right and right-to-left shunts at both atrial and ventricular levels.

It is concluded that the usual circulatory pattern in cases of the "pure" type consists of a left-to-right shunt at the atrial level exactly balanced by a shunt in the opposite direction—aorta to pulmonary artery—through the ductus. The atrial shunt can probably be easily established in the presence of an actual defect of the atrial septum. When only a patent foramen ovale is present, however, it may have to await cardiac dilatation and stretching of the foramen ovale until the protecting "valve" is no longer competent. This appeared to be borne out by anatomical observation in two of the "pure" cases in which autopsy was done. If the atrial defect is large enough, a mixed shunt may occur. In this case the left-to-right shunt must exceed the right-to-left by exactly the value of the aorta-to-pulmonary artery shunt through the ductus.

Periodic reversal of shunt or intermittency of shunt, as described by Taussig, could not be demonstrated in these cases.

These infants did not have lessened cyanosis in the lower extremities as compared with the upper extremities, nor did they present any demonstrable physiological mechanism (pulmonary artery to aorta shunt through the ductus) which could result in this clinical observation.

DISCUSSION

DR. GLADYS J. FASHENA, DALLAS: I don't know how to explain it, but difference in the degree of cyanosis of the hands and feet has been a common finding in our patients with this anomaly. In a series of seven patients proved to have transposition of arterial trunks by either autopsy or angiocardiography, six showed appreciably more cyanosis of the hands than of the feet. None of these had any interruption of the aortic arch. We have considered the finding to be helpful diagnostically.

DR. R. E. L. FOWLER (by invitation), New Orleans: We anticipated this comment and have no explanation except that we have not been lucky enough to find a case which illustrates this up to the present point. However, the importance of the exact understanding of the basic factors involved in congenital heart disease has become apparent to all of us, I think most strikingly through the development of the Blalock-Taussig procedure for the alleviation of pulmonic stenosis.

Transposition of the great vessels is another relatively common congenital cardiac anomaly in the neonatal age group carrying even a worse prognosis than that of pulmonic stenosis. We hope that this and similar studies may be of value to those now actively engaged in seeking a successful surgical approach to the correction of transposition of the great vessels.

Study of the Duodenal Fluid in Infants with Jaundice. DR. PAUL PATTERSON (by invitation), Boston.

A study of the bile-free duodenal fluid of a child with a surgical biliary fistula disclosed a fluid of abnormally increased viscosity and reduced trypsin which could not be enhanced by the addition of the patient's bile. However, after surgical reshunting of the bile into the duodenum, the fluid returned to normal viscosity and tryptic activity.

An analysis of the duodenal contents in 35 cases of biliary obstruction revealed that the occurrence of scant, viscid fluid with reduced or complete absence of trypsin was associated with the absence of bile.

An examination of the fluid aspirated from the duodenum of infants with pancreatic fibrosis given intravenous sodium dehydrocholate (decholin sodium®) disclosed a marked increase in volume of duodenal fluid and a decreased viscosity. The trypsin remained absent.

Accordingly, 10 infants with obstructive jaundice of 5 to 25 weeks' duration were studied in this fashion. They likewise had complete absence of bile, increased viscosity, and absence to definite reduction of trypsin of their duodenal fluid. They received intravenous injections of 2 to 5 ml. of 20% sodium dehydrocholate and oral bile salts (ketochol®). Bile was demonstrated on duodenal intubation of three after but one injection (one after aspiration of a bile-stained mucus plug). Five had bile present within 7 days, the other two at 14 and 21 days. Four were confirmed to have normal extrahepatic ducts by surgery, by inspection, and by roentgenography with iodized oil U.S.P. injected into these ducts. Clinical improvement followed, with loss of jaundice, fall of bilirubins, restoration of yellow stools, and clearing of urine of bile and albumin. Gelatin film tests for stool trypsin which previously gave negative results now gave positive results. One child's treatment was stopped prematurely, and the child is now jaundiced with cirrhosis of the liver. Another died one month later of unknown cause (suspected cholangitis) but had no jaundice. One other is jaundice free but suspected to have cirrhosis of the liver. Surgical exploration was performed on these three.

Cause of jaundice is explained on loss of intrahepatic biliary pressure and bile stasis as a result of cellular destruction and dysfunction caused by Rh and blood group A-B-O incompatibility with hyperimmune antibodies demonstrable in the mother's blood (four cases); liver anoxia as a result of cyanosis and dyspnea in the neonatal period (three cases); severe unexplained anemia (one case); unexplained hepatitis with inspissated bile confirmed by biopsy (two cases). One patient had a mucus plug of the extrahepatic system. All patients had normocytic, normochromic anemia, as did the patients with true biliary atresia.

Six additional cases of jaundice of two to three weeks' duration were proved to be obstructive, and all patients were infants with erythroblastosis who had not received adequate therapy, such as exchange transfusions. These responded readily to the first injection of sodium dehydrocholate, but one took four days to have free flow of bile.

Thirteen additional patients with obstructive jaundice were treated, with failure resulting. All had congenital absence or atresia of extrahepatic ducts at surgery.

Since surgery promises very little in cases of true biliary atresia and may aggravate these cases of intrahepatitic disease, it is recommended that in cases of jaundice persisting over three weeks in the neonatal period, partial or complete intrahepatic or extrahepatic obstruction should be suspected, and that this mode of therapy plus blood transfusions should be instigated and tried for at least three weeks before surgery is undertaken.

DISCUSSION

DR. COOKE, New Haven, Conn.: We had a case somewhat similar to this, except that there was no elevation of the serum bilirubin at any time, although the alkaline phosphatase was tremendously elevated at all times. On first exploration of the patient, there was no evidence of obstruction of the biliary tract. On reexploration, a very definite narrowing of the biliary system was found, and at postmortem examination, which occurred shortly after the second exploration, there was found some bile stasis in the canaliculi, although there was at no time an elevation of bilirubin.

DR. DOUGLAS JOHNSTONE (by invitation), Baltimore: I want to congratulate Dr. Patterson on his fine work. We have been interested for some time in the trypsin aspect of this study and have studied jaundiced patients for their duodenal and stool trypsin. I have in mind a child with biliary atresia who appeared to have normal stools at birth; these subsequently became gray, and whereas he had had normal trypsin, shortly after birth he had a complete absence of trypsin as his stools became gray.

I remember also a child with cirrhosis of the liver complicated by diabetes mellitus who also had diminished trypsin.

Not to get off the subject, I should like to make one comment on this viscosity metric method of studying so-called partial cystic disease in patients with pancreatic disease. I think it is true that there may be such an entity as partial cystic fibrosis of the pancreas, and we might be able to pick up these cases by the viscosity method before the diagnosis is proved. However, I am reminded of the patient in Bellevue who was thought to have cystic fibrosis of the pancreas because of the very viscous duodenal juice and typical clinical history. However, the duodenal juice showed, by the Anderson method, a "lower limit of the normal trypsin," and stool tests showed a "positive reaction for trypsin"; consequently, the diagnosis of pancreatic fibrosis which had been entertained was ruled out. The child died and was found to have died of Ps. aeruginosa pneumonia, and he did have cystic fibrosis, as shown on postmortem examination.

So, I think, again, the soy bean trypsin inhibitor should be used in these instances of viscous duodenal juice, so-called partial cystic, to prove it is trypsin and not gelatinase that is causing the results in these tests.

DR. SYDNEY GELLIS, Boston: I think that it is definite that many of the cases that we have had in the past and diagnosed as atresia of the bile ducts have turned out to be just the sort of problem that Dr. Patterson has mentioned. All of us have seen patients that have come to surgery, been declared inoperable, and had subsequent disappearance of jaundice.

I think that what happens is that certain of these children have very small bile ducts and might perhaps never get into trouble but for the fact that in the first few days afer birth they have a combination of increased bilirubin plus relative dehydration, combining to give sufficient stasis and thickening that they then have a picture of apparent atresia of the bile ducts. The operation and manipulation of the bile ducts are sufficient to dislodge the bile and get the flow started.

DR. PAUL PATTERSON (by invitation), Boston: I think we should recognize that cases of this type of jaundice, whether hemolytic or obstructive, are very difficult to diagnose, and, with Dr. Cooke, we have seen some cases of complete atresia in which the bilirubins have been very, very low and some of partial obstructions in which the bilirubins have been very high. You certainly cannot go by the mother's word. In the case of one child 6 months old, said to have been jaundiced since birth, the mother said the jaundice was improving because the child was no longer yellow, it was now green. He was one in our series that we did relieve of an obstruction.

But in seeing these children, I think it is worth while, for any jaundiced baby, to do these tests for antibodies, to recheck Rh factor, specifically in the mother's blood, and to give the child a course of treatment before presenting it to surgery, because I feel definitely that the surgery lessens the chance of these children and I definitely think they will improve better on the medical regimen laid out for them.

News and Comment

ANNOUNCEMENTS

Coming Examinations to Be Held by the American Board of Pediatrics, Inc.—The American Board of Pediatrics, Inc., will hold oral examinations on Feb. 1, 2, and 3, 1952, in New York and on March 21, 22, and 23, 1952, in St. Louis.

GENERAL NEWS

Specialists Certified by the American Board of Pediatrics, Inc.—The following physicians were certified as specialists by the American Board of Pediatrics, Inc., after examinations held in Buffalo on Oct. 26, 27, and 28, 1951:

Ahari, Hassan, Teheran, Iran.
Arnoult, Mathew Blake, Memphis.
Bastedo, Donald Lou Alexander, Kitchener, Ont., Canada.
Baybutt, John Edward, Easton, Md.
Burke, Edmund Charles, Rochester, Minn.
Burr, Charles L., Des Moines, Iowa.
Christensen, Charles Neil, Springfield, Ill.
Cooper, James Oliver, III, El Dorado, Ark.
Davidson, Douglas T., Jr., Boston.
Davis, Herbert Van Dyke, Kansas City, Mo.
Drinker, Henry Middleton, Philadelphia.
Eiser, Joseph, Los Angeles.
Farquhar, John Denney, Drexel Hill, Pa.
Field, Edward Graham, Glen Burnie, Md.
Fine, Irving, San Carlos, Calif.
Ford, John H., Jr., Binghamton, N. Y.
Greenfield, Stanley S., Brooklyn.
Groff, Frederick A., Jr., Schenectady, N. Y.
Hamilton, George Livingstone, Jr., Lawrence, Mass.
Harned, Herbert Spencer, Jr., Hamden, Conn.
Heller, Theodore M., Brooklyn.
Howard, Fred Hiland, Milwaukee.
Hsu, Ching-feng, Hong Kong, China.
Keen, Sol Norman, New York.
Kennedy, Charles, Philadelphia.
Kennedy, Sidney R., Jr., Torrington, Conn.
Kokomoor, Marvin L., Gainesville, Fla.
Larsen, Jean West, Middletown, N. Y.
Leppla, Bruce William, Lompoc, Calif.
Lomas, Robert Dawson, Houston, Texas.
McAuliffe, Vincent J., Teaneck, N. J.
Mascia, Armond Vincent, Tarrytown, N. Y.
Matlin, Melvin, Poughkeepsie, N. Y.
Mazursky, Milton Michael, Roselle, N. J.
Mehlman, Julia, New York.
Miller, Robert Warwick, Rochester, N. Y.
Monroe, Robert W., Greenville, Pa.
Mullen, Francis Newby, Jr., Norfolk, Va.
O'Neal, Ruth, Winston-Salem, N. C.
Samuels, Irving Leonard, New Rochelle, N. Y.
Scarano, Jenaro Gerardo, Ponce, P. R.
Schulman, Irving, New York.
Spencer, Harrison Clark, Abingdon, Va.
Stabins, Edwin Paul, Charleston, W. Va.
Standard, Ruth Esther, Germantown, Pa.
Stein, Felix, Brooklyn.
Sternberg, S. David, Brooklyn.
Stowens, Daniel, Camp Cooke, Calif.
Sullivan, Albert William, Rochester, N. Y.
Sylvester, Robert F., Jr., Columbus, Ohio.
Tabrah, Frank L., Bellingham, Wash.
Vaughan, Victor Clarence, III, New Haven, Conn.
Waters, William J., Syracuse, N. Y.
Woolington, Samuel Swartz, Long Beach, Calif.
Zimmerman, John Harvey, Greensburg, Pa.

Specialists Certified by the American Board of Pediatrics, Inc.—The following physicians were certified as specialists by the American Board of Pediatrics, Inc., after examinations held in Chicago on Nov. 30 and Dec. 1 and 2, 1951:

Benton, John J., Panama City, Fla.
Biehusen, Frederick Charles, Tacoma, Wash.
Borenstine, Joseph, Kansas City, Mo.
Bosley, Warren Guy, Grand Island, Neb.
Branthaver, Charles Augustus, Sacramento, Calif.
Brownlee, Robert C., Jr., Anderson, S. C.
Buchanan, Gibson Packer, Pittsburgh.
Chang, Charles Chi, Dallas, Texas.
Clapp, Roger W., Butte, Mont.
Cohen, Lawrence Joseph, Cheyenne, Wyo.
Colon, Wildo D., Shreveport, La.
Currence, William Ward, San Antonio, Calif.
Davis, William S., Denver.
Deisher, Robert William, Seattle.
Eiben, Robert M., Cleveland Heights, Ohio.
Eisen, Herman Murray, Los Angeles.
Ellenburg, Luke L., Greenville, Tenn.
Engle, Mary Allen English, St. Louis.
Farrell, Harry William, Sioux Falls, S. D.
Featherston, William Matthew, Elk City, Okla.
Forgrave, Edward George, Detroit.
Freeman, Gerald I., St. Paul.
Garrisi, Joseph A., Montebello, Calif.
Grabau, Gene H., St. Louis.
Gross, William V., Jr., Baltimore.
Hellyer, David Tirrell, Tacoma, Wash.
Hicks, Alfred, II, Denver.
Holliday, Pope B., Jr., Chattanooga, Tenn.
Jones, Isabel Essig, Berkeley, Calif.
Kagen, Gordon Arthur, Reading, Pa.
Kasmersky, Chester T., Columbus, Ohio.
Ketchum, William F., Baton Rouge, La.
Kishner, Leonard L., Tulsa, Okla.
Kravitz, Harvey, Chicago.
LaBranche, Hernandez Gustave, Fort Leonard Wood, Mo.
Liss, Emanuel C., South Bend, Ind.
Logan, Richard Seymour, Elkhart, Ind.
Lynch, Franklin, Westport, Conn.
McCammon, Robert William, Denver.
McClelland, Charles Q., Captain, Medical Corps, United States Army.
Mewhinney, Logan U., Dallas, Texas.
Mudgett, Roxie Tyler, Louisville.
Munsey, Franklin Albert, Rockford, Ill.
Patton, James Moss, Spokane, Wash.
Peterson, Floyd Russell, Los Angeles.
Reinhart, John Belvin, Winston-Salem, N. C.
Rothenberg, Lionel H., Houston, Texas.
Schroeder, Albert John, Minneapolis.
Shen, Jerome T. Y., St. Louis.
Speer, Frederic, Kansas City, Kan.
Steigerwalt, John Latshaw, Rosemont, Pa.
Van Biber, James T., Independence, Mo.
Vangrov, Stanley, Dayton, Ohio.
Webb, Bailey, Durham, N. C.
Whittemore, James P., Portland, Ore.
Zirkle, George Andrew, Jr., Knoxville, Tenn.

Book Reviews

Researches on the Measurement of Human Performance. By N. H. Mackworth. Medical Research Council Special Report Series No. 268. Price, 4 shillings. Pp. 156, with 58 figures and 1 plate. His Majesty's Stationery Office, York House, Kingsway, London, W.C. 2, 1950.

In 1943 the Royal Air Force asked for laboratory studies that might determine the optimum length of time radio operators in antisubmarine patrols should be kept at watch. This request was made because of evidence that during patrols numbers of potential U-boat contacts were being missed. This report records visual and auditory vigilance tests, in which the conditions under which men actually operated during watch to detect signals indicating presence of enemy underwater craft were simulated.

Auditory vigilance tests were also devised and apparatus designed to provide a test simulating the duties of Asdic (sonar) operators. Asdic equipment detects presence of submerged submarines by providing an auditory signal representing the echo reflected by underwater objects.

In all the tests the conclusions were that subjects miss more signals after working one-half hour and that the decline can be prevented by alternation of this duty with other work at one-half-hour intervals.

Supplying knowledge of results during the test prevented the decline. Amphetamine (benzedrine®), 10 mg., when taken one hour before the test maintains the initial level of accuracy over the two hours of the test. High temperature unfavorably affects the accuracy of response. It is concluded that some central cerebral process, rather than any local alteration in functioning of the peripheral sensory mechanisms, auditory or visual, is involved in the alterations in behavior observed.

A second series of tests were directed toward investigation of effects of environmental stress on effectiveness of performance. The effects of nonlethal war gases and of high atmospheric pressures were studied. Subjects were exposed to tear gas, arsenical smoke, or were required to do heavy manual work or highly skilled work (a wireless telegraphy reception test) at high temperatures. It was determined that for all forms of intensive work, physical or mental, there is a critical region on the atmospheric-temperature scale above which effective work is not done. A meticulous inquiry into the nature of this deterioration is presented.

This work is an important contribution to methodology in the investigation of efficiency of performance. Its practical significance seemingly will be enhanced, in view of the present likelihood that those same tasks originally calling for investigation again become important in relation to national security. The observations, however, have a wide field of application in all inquiries into factors that increase or decrease the efficiency of workers at tasks requiring large energy expenditure, whether the task be a physically demanding one or one that calls for vigilance and a high degree of skill.

Principles of Human Genetics. By Curt Stern. Price, $7.50. Pp. 628, with 198 illustrations. W. H. Freeman and Company, 549 Market St., San Francisco, 1949.

Within the last 20 years the physician has been forced to recognize the importance and outstanding role that heredity plays in his busy practice. The advent of antibiotics and chemotherapy, preventive medicine, and so forth has done much to lighten the infectious burden in medicine, but this only to confront the profession with an apparent increase in developmental as well as geriatric hereditary disease. The great majority of American physicians do not possess the background requisite to correct interpretation of the voluminous and rapidly expanding genetic literature. This lack of educational background is largely the result of the paucity of formal courses in human genetics in our major medical school curricula. While the relatively new and meteoric science of human genetics is not difficult to understand, it does require diligent

application and study. To aid the physician, as well as the medical student, to acquire the principles and a knowledge of hereditary patterns, there is now available a most satisfactory text for the study of human genetics.

"Principles of Human Genetics" is a masterfully written text for students of human heredity. The material is assembled into twenty-seven chapters. The author very cleverly intersperses chapters dealing with interaction between genes and substrates, cleavage and differentiation, and the development of syndromes between those dealing with mitosis and meiosis. This admirably serves the purpose of the author to keep up the "reader interest" of the student. The fundamentals of probability, single-factor inheritance, and lethal genes are covered in Chapters 5, 6, and 7. The illustrations are good, and the example problems for student exercise are representative.

Chapter 8, concerned with "Problems of Genetic Advisors," is most important to the student of human genetics. The need for competent consultants in human genetics is stressed.

Chapters dealing with "Genetic Rations," "The Hardy-Weinberg Law," and "Multiple Alleles" follow in easily digestible form. The arithmetic necessary for understanding this material is presented in a most comprehensible and lucid manner.

Medicolegal genetics is outlined in Chapter 12 and again stimulates the appetite of the interested reader and student. The importance of serological aid in ascertaining paternity in legal cases is emphasized.

Human linkage is clearly and expertly expounded in Chapter 13.

Material on irregular expression of genes and prenatal interactions is easily read and understood, and this is most important in that it is most necessary to an understanding of human genetics.

Multifactor inheritance, at best a difficult subject, is originally and skilfully handled, as is the material dealing with consanguinity. The author brings about the interesting and sensibly expected forecast that in the future we will be able to provide palliation and modification of the action of our noxious genes.

The chapter on sex ratio is meticulously written.

The relation of heredity to environment, long a controversy, is skilfully illustrated in that the author employs twin studies to expound both the genetic and the environmental contribution to variability of human pathology.

The discussion of selection and eugenics and the two chapters assigned to races of man stimulated the reviewer, as they will the student, by their mature and conservative treatment.

The concluding chapter deals with the evolution of man and the primates. The author intriguingly suggests that man may, in the future, control to a large measure his own biological evolution.

Your Deaf Child. By Helmer R. Myklebust. Price, $2.50. Pp. 133, with pen sketches. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill., 1950.

This book is written expressly for the parents of deaf children and can be enthusiastically recommended for its authoritative background, excellent writing, and thorough coverage of the problems associated with hearing impairment in childhood. There is constant emphasis on parental understanding as a prerequisite to normal personality development in the handicapped child.

Among the chapter headings are included the meaning of deafness, its causes and types, parental attitudes and their significance, the needs of the deaf child, the acquisition of ability by the child to take care of himself, problems of communication, and what may be expected of the child. There is also a section devoted to the organizations which can help, pertinent books and periodicals, and a list of schools for the deaf and hard of hearing in the United States and Canada. The publisher's usual high standard of book presentation adds even more stature to this fine volume. The reviewer wishes that some way could be found to make this book available to all parents of deaf children.

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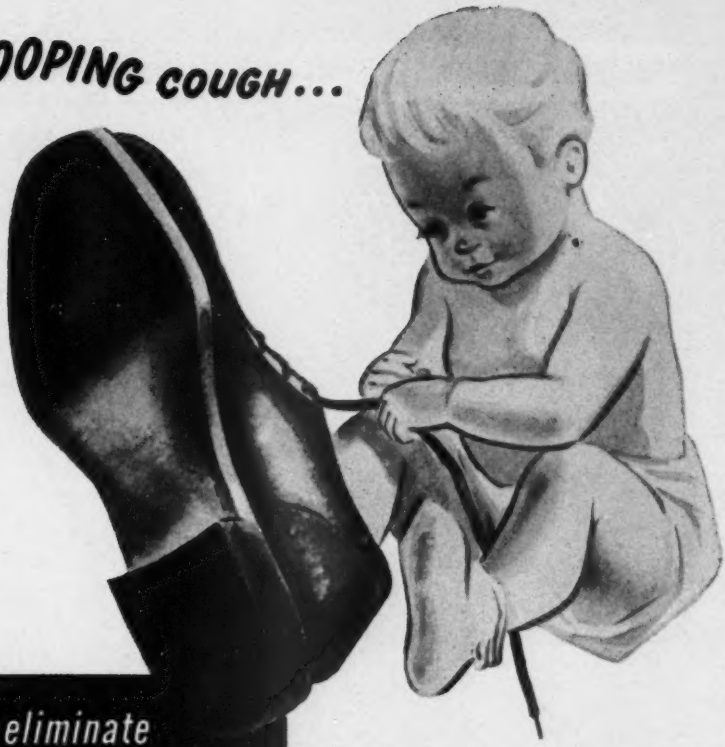

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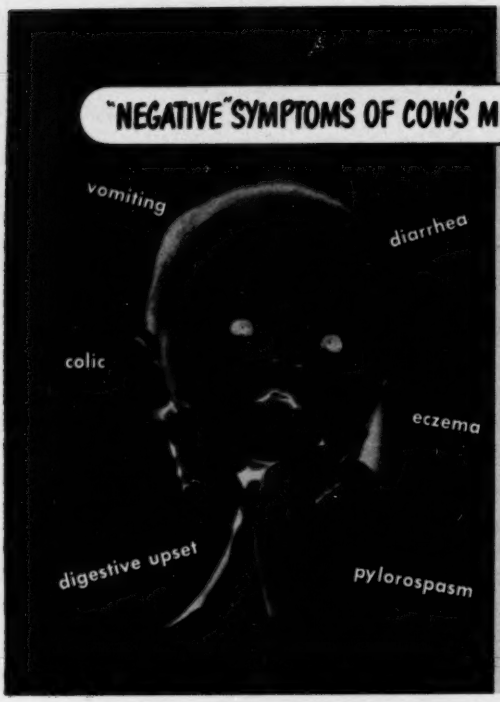

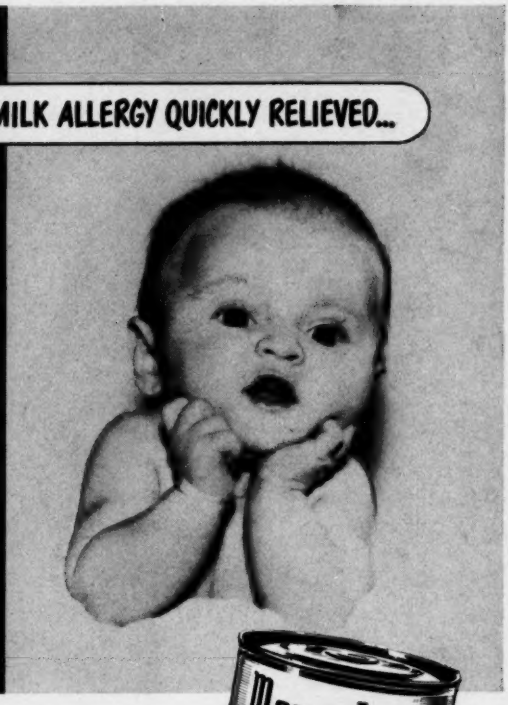

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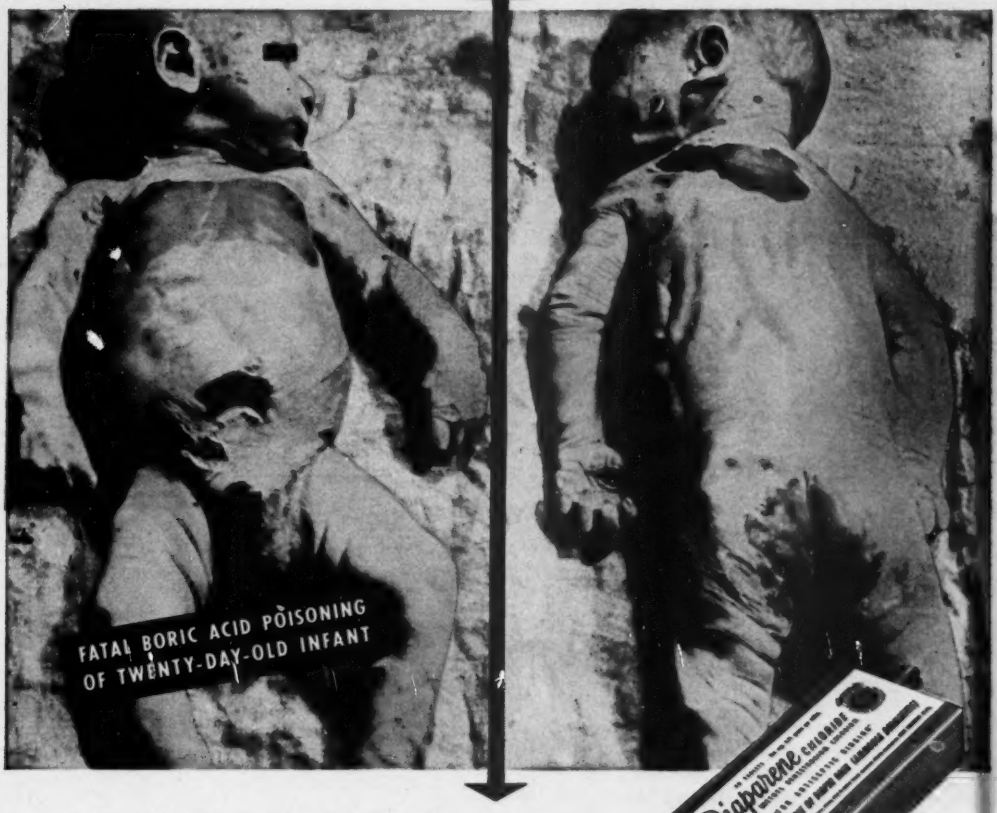

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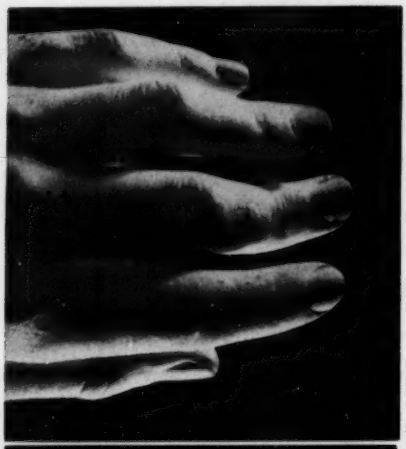

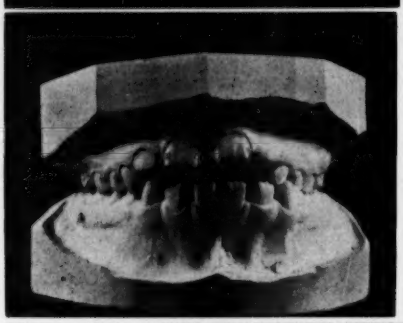

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*Jeans and Marriott, "Infant Nutrition"—4th Edition, Page 74.

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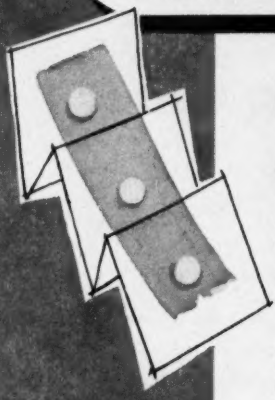
SOLTABS®

CRYSTALLINE PENICILLIN G POTASSIUM



EFFECTIVE ORALLY IN MANY ACUTE INFECTIONS

Soltabs are soluble tablets molded directly from crystalline penicillin G potassium, without added diluents. They are available in two potencies, 50,000 units and 100,000 units, each tablet individually sealed in foil.

The oral administration of Soltabs shows two important advantages over parenterally administered penicillin: the incidence of side reactions is reduced* and the psychic trauma of repeated injections is avoided.

IN INFANTS AND CHILDREN

For infants, the average therapeutically effective dose is one 100,000 unit Soltab, dissolved in two ounces of formula, given every three to four hours.

For older children the average effective dose in scarlet fever, tonsillitis, otitis media, pneumococcic infections and Vincent's angina is 200,000 units every three or four hours, dissolved in two ounces of milk or fruit juice, or in a spoonful of ice cream, jelly, or honey.

IN ADULTS

For adults, too, Soltabs find excellent use. Orally, they are easily swallowed with water or any other liquid, and they lend themselves well to aerosol administration. While dosage is about five times the parenteral dose, only a small amount of penicillin by weight is required; hence dosage requirements are never so high as to make the cost prohibitive.

Soltabs are supplied in two potencies, 50,000 and 100,000 units each, in boxes of 24 and 100, each tablet sealed in foil.
Your wholesaler is stocked, order your supplies now.

*Keefer, C.S.: Evaluation of Antibiotic Therapy, Postgrad. Med. 9:101 (Feb.) 1951.

C.S.C. Pharmaceuticals

A DIVISION OF COMMERCIAL SOLVENTS CORPORATION • 17 EAST 42ND STREET, NEW YORK 17

From here on...

Right from the first feeding, 'Dexin' may be added to the infant's formula with the assurance that it is not liable to cause fermentation and discomfort.

'Dexin' is composed of 75% dextrins and 24% maltose. The small amount of maltose is quickly assimilated. The dextrins are not fermented by the usual intestinal bacteria. This *does* make a difference in comfort to the baby.

'Dexin'® brand High Dextrin Carbohydrate

Tins of 12 oz. and 3 lbs.

6 level-packed tablespoonfuls of 'Dexin' = 1 oz. = 115 calories.

Burroughs Wellcome & Co. (U.S.A.) Inc. *Tuckahoe 7, New York*

A tradition in infant feeding for 20 years

the quality and dependability of PABLUM cereals

A MULTI-GRAIN cereal and three single-grain cereals share the Pablum® heritage of quality.

Uniform texture and maximum digestibility as well as high nutritional values are assured by careful Pablum processing.

Vitamins and minerals from natural sources are incorporated in Pablum Mixed Cereal, Pablum Oatmeal and Pablum Barley Cereal. Pablum Rice Cereal, enriched with crystalline vitamins, has special advantages of hypoallergenicity.

Recent improvements in Mead's exclusive manufacturing process bring out more than ever the rich, full grain flavors of all the Pablum cereals.

Older children as well as infants will like these 4 cereals and welcome the variety they provide.

You may prescribe Pablum cereals with *confidence*.

The Pablum packages, designed for superior protection and convenience, have the exclusive "Handy-Pour" spout.

MEAD'S

MEAD JOHNSON & CO.
EVANSVILLE 21, IND., U. S. A.

clinically accepted

for
increased safety
high degree of efficacy
excellent palatability

in triple
sulfonamide therapy

council-accepted

tri-sulfameth

Each 5 cc. (approx. one teaspoonful) of syrup or each tablet provides:

Sulfamethazine	0.165 Gm.	(2.5 gr.)
Sulfadiazine	0.165 Gm.	(2.5 gr.)
Sulfamerazine	0.165 Gm.	(2.5 gr.)
Sodium Citrate*	0.5 Gm.	(7.7 gr.)

*not contained in Tri-Sulfameth Tablets

"Trials of sulfonamide combinations . . . have indicated that the occurrence of crystalluria can be decreased to negligible proportions." Virginia Medical Monthly 75:56, 1949.

PROFESSIONAL SAMPLES ON REQUEST

casimir funk laboratories, inc.
affiliate of U. S. Vitamin Corporation
250 East 43rd St., New York 17, N. Y.

Dispersible

DRISDOL®

WITH

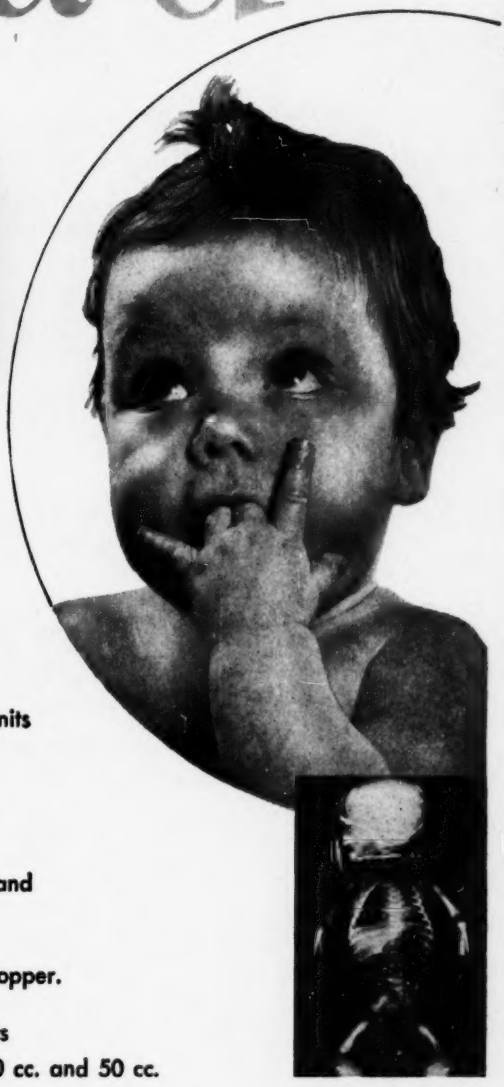
VITAMIN A

COMPLETELY

Milk

Diffusible

a+d



Drisdol with Vitamin A administered in milk becomes an integral part of the child's diet. It diffuses completely in milk, orange juice and other liquids without an oily film, does not separate, float or tend to adhere to nursing bottle or nipple. May also be given on the tongue or in solid foods.

Drisdol with Vitamin A contains per gram 50,000 units of vitamin A and 10,000 units of crystalline vitamin D_2 (calciferol). Each drop delivers 1250 vitamin A units and 250 vitamin D units.

Dosage for infants, 2 drops; for older children and adults, from 4 to 6 drops daily in milk.

Supplied in bottles of 10 cc. and 50 cc. with dropper.

Also Drisdol in Propylene Glycol (10,000 units of vitamin D_2 per gram) in bottles of 5 cc., 10 cc. and 50 cc.

To help build a sound structure and promote growth

Drisdol, trademark reg. U. S. & Canada, brand of crystalline vitamin D_2 (calciferol)

Winthrop-Stearns INC.

NEW YORK, N. Y. WINDSOR, ONT.